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CONGENITAL ADRENAL HYPERPLASIA FAMILY CONFERENCE LEEDS 10TH MAY 2009

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CAH IN CHILDHOOD

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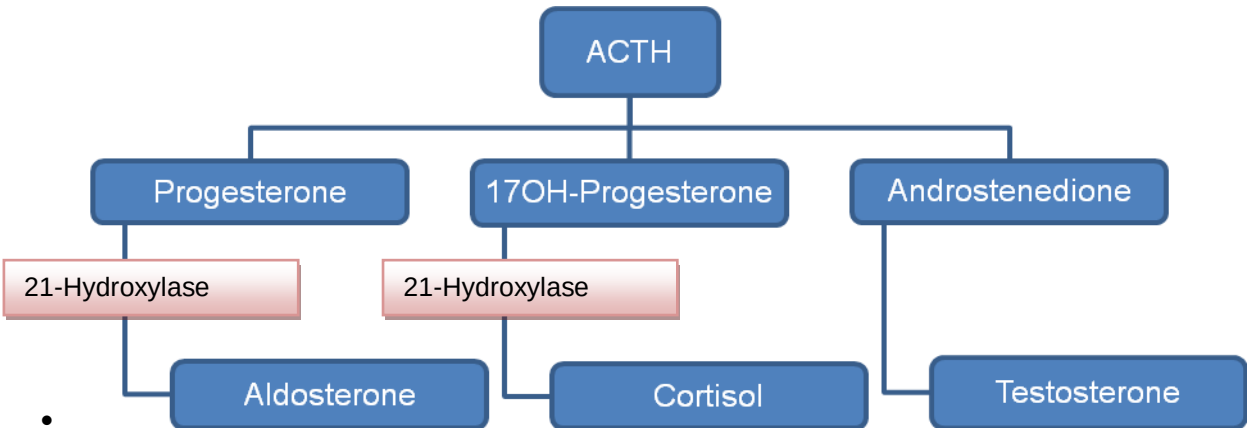
LEEDS GENERAL INFIRMARY

CAH IN CHILDHOOD

The pituitary gland in the brain makes the hormone ACTH, which stimulates the adrenal glands. These are two triangular structures which sit on top of the kidneys and are responsible for making the hormones which control daily functions.

- **Mineralcorticoids** control salt and water balance
- **Glucocorticoids** control sugar
- **Androgens** – of which the main one is testosterone which can be converted to oestrogen



21-hydroxylase is the most common form of CAH. As can be seen in the diagram above, if we get the block at that level, there are resultant reductions in aldosterone and cortisol. Lack of aldosterone leads to salt loss, vomiting, and poor growth, whilst cortisol deficiency results in low sugars and lethargy. The resultant impaired negative feedback loop leads to an increase in ACTH trying to drive through the aldosterone and cortisol pathways to compensate. Due to the block, they are effectively "shunted off" leading to an increased amount of testosterone in the body. The excess testosterone results in faster growth, hair growth and signs of puberty.

A couple of quick definitions:

- **Androgens** – general name for any male hormone e.g. testosterone, androstenedione.
- **Androgen excess/virilisation** – increasing pubic or body hair, enlarged penis or clitoris, change in voice, male type baldness

CAH is an inherited condition where children are born with enlargement of the adrenal glands. It has an incidence of approx 1 in 15,000 - there is an ongoing survey at present within the British paediatric community looking at the true incidence around the country. CAH is an autosomal recessive condition, which means that two copies of an abnormal gene are required to manifest the condition.

Future children of a couple with CAH have a 1 in 4 chance of being affected, and a 1 in 2 chance of being carriers. The carrier rate in the general population is approximately 1 in 50.

Infants present with indeterminate genitalia (females) or become suddenly unwell and have a salt losing crisis.

TYPES OF CAH

- **Salt losing** – 2 severe mutations (<1% of normal 21-OH activity)
    - Girls – virilisation at birth
    - Boys – detected within first 2 weeks of age typically. Symptoms will include poor feeding, vomiting, and lethargy.
- **Simple virilising**. Typical presentation at 2-4 years of age. Both boys and girls, tend to present with pubic hair, acne, sweatiness and faster growth progression. Both sexes develop an earlier puberty due to early exposure of the brain to sex hormones (priming).
- **Late onset**. Tends to be in females from adolescence onwards. May present with PCOS type syndrome, acne, irregular periods. I won't be covering this type today.

Females require an endocrine and surgical review as soon as possible. Psychological input is offered. To get to the diagnosis, bloods are taken, ultrasound scans are conducted, and chromosomes examined. Discussions are then held with the family, and the sex of the baby assigned.

TREATMENT

The treatment goals are to replace the missing steroids, minimise excess steroid production (i.e. testosterone), avoid over-replacement, to prevent weight gain, minimise virilisation, and optimise final height.

Treatment is based on surface area. In the first few months a higher dose may be required, which can be reduced once the 17OHP levels are suppressed.

Typical dosing:

- **Hydrocortisone** – 10-20mg/m^2/day – three times a day, generally with the highest dose given in the morning
- **Fludrocortisone** to help with the salt and water balance – 100µg (1 tablet) once a day (the dose may vary between 1 to 3 tablets)
- **Sodium chloride** during the first year

Hydrocortisone is not perfect as you can't adequately match the normal cortisol production – i.e. the circadian rhythm. The last dose is given late at night, not necessarily when the cortisol is required, but to maintain some cortisol presence throughout the night.

3 main steroids are used.

- **Hydrocortisone** is usually given thrice daily, with the highest dose in the morning
- **Prednisolone** – 4x the potency of hydrocortisone, sometimes used at night time in older children due to the longer half life
- **Dexamethasone** is very potent and not used in children. A useful trait of this is that it crosses the placenta and can be used to treat pregnant mothers to prevents virilisation of a female infant

STEROID TREATMENT DILEMMA

- **Height** - Too low a dose results in rapid initial growth, but decreased final height. Too much suppresses growth.
- **Weight** - Over treatment results in obesity. Under treatment can lead to earlier maturation (puberty) and increased virilisation.

MANAGEMENT OF ACUTE ILLNESS

If a child has an intercurrent illness, but is generally well, then double the dose of hydrocortisone. If they are unwell with a fever, triple the dose.

If their illness is more severe than this, with increasing lethargy, diarrhoea, vomiting / fractures then give a hydrocortisone injection and proceed to hospital.

AT LEEDS – SPECIALITIES

At Leeds, if we have a child that is just diagnosed, then either myself or my colleague will see them. We will see them jointly with the surgeon within the first couple of days, and we will bring them back to a joint surgical clinic for a discussion. Our general recommendations are to avoid surgery in the first year, and often to delay this till much older.

In the first few months we tend to have a follow up with our geneticist, who provides advice on screening, future children, and counselling.

Dr Orme (adult endocrinologist) gets involved around adolescence, for the transition to adult services, and they will be seen there for the best part of 1 or 2 years. Around adolescence, there are joint clinics with Prof Balen, for discussions on future adult surgery.

In males, during development, cells from the adrenal glands can get left in the testes. With CAH these cells grow as well, and can potentially impair the future functioning of the testes. These are known as Testicular Adrenal Rest Tumours (TARTs), despite the name they are not in actual fact malignant.

MONITORING

The standard blood test for monitoring is the 17OHP, but this is a stress hormone and can vary several fold during the day. Some places also do androstenedione and testosterone, which tend to be more stable in the blood. 17OHP can also be tested in saliva, but this is only viable at around 5 years when children are old enough to spit! Renin is also monitored to assess if adequate fludrocortisone is being given.

Other indicators include weight, height, blood pressure, puberty/periods, and bone age.

BONE AGE

Bone age assesses the skeletal age – you only stop growing once your bones fuse. Generally, an advanced bone age indicates less growth potential, and indicates an excess of androgens, i.e. poor control.

Very advanced bone ages tend to be present in simple virilising cases, as they present later. A typical scenario for such a child would be that they are tall, but with a bone age several years in advance of their chronological age. This potentially results in a reduced final height.

ADDITIONAL THERAPY

If we find that the child is in early puberty, we can stop this using GnRH, which works at the level of the pituitary gland, and stops puberty for a number of years until they are an ‘average’ age to undergo puberty.

Growth hormone is sometimes used to improve height potential if there is the possibility that the child could end up very short. Finally Aromatase inhibitors can block conversion of testosterone to oestrogen, and thus may limit skeletal maturity, however this should only be considered ‘experimental’ at the moment.

PRE-NATAL MANAGEMENT

The rationale of this is to treat the foetus via the mother to prevent the genital manifestations. This is done by starting dexamethasone treatment in the first trimester. A Chorionic villus biopsy is conducted around 10 weeks, and the treatment is continued if the test indicates an affected female. Only 1 out of 8 mothers need to continue treatment.

SUMMARY

CAH needs a multi disciplinary approach. There needs to be support, and accessibility to all members within the team. There are different priorities for all families, and vigilance is needed for age specific issues as they arise.

Q&A

1. ***How accurate is the bone age x-ray examination as a determination of the actual bone age? Is there a wide variation in reading? The reason I ask is that I have a child who seems to be absolutely on the nail in every other area of control, but the bone age seems to be accelerating.***

   A trend is better is better than a single value. It is not unusual to have variation of around 1 year from the child's age. Differences may arise depending on the bone age atlas that is used to report the scores and on the expertise of the reporter. It is important that the same individual reports the bone age using the same methodology.

   So what is the largest tolerance band you can expect on a bone age then?

   There are too many variables to be able to answer that really. As long as the same person does the reporting, using the same atlas, and you obtain the trend from that, it should not be an issue. Most of the endocrine bone ages are reported by the consultants [at Leeds].

2. ***What age do you start doing bone age scans?***

   Generally around 4-5 years, unless signs of early puberty have been noted before then, in which case they would be very useful. Generally the accuracy decreases with decreasing age.

3. ***So at what frequency should bone age be checked?***

   Everyone uses different criteria. If they are growing well, I would only do a bone age every 2 years.

4. ***Does fludrocortisone make you retain potassium or shed potassium?***

   Shed potassium.

5. ***So what is the trend generally that you see on potassium levels? My child has very low potassium normal levels, barely making normal levels. Is that normal for children on fludrocortisone, or does that indicate too much, or another problem*?**

   It may indicate that they are on too much, you have to look at the sodium level too, and their blood pressure as well.

   They're both fine, but he never gets beyond 3.7, and that has been over several years. He never makes it up to 4.

   I would consider 3.7 in the normal range. There is a variation from 3.5 to 4.5.

6. ***How would you act if a child was declining quite rapidly compared to the cortisol circadian rhythm chart in the morning.***

   You will never be able to match the normal rhythm; we can only mimic it as closely as possible. Taking the other factors of height, weight, androgen levels, and if there were signs of virilisation, i.e. there was a trend that you were losing control, then I may look at prednisolone in an evening dose.

   We just started that a couple of days ago, there was quite an increase in virilisation, and a 24 hour profile showed that between 2 and 5 her levels were causing the problems.

7. ***What is the difference between saliva testing and bloods?***

   They will both give you a similar answer.

8. ***My son just takes the same dose of hydro three times a day. I was interested to see that some people were taking a higher dose in the morning or evening. Does anyone else take the same dose? He is on 7.5mg.***

   The hydrocortisone tablets can only be reliably split to 2.5mg.

CAH IN ADULTS

DR STEVE ORME

CONSULTANT ENDOCRINOLOGIST

LEEDS GENERAL INFIRMARY

HORMONE REPLACEMENT – GLUCOCORTICOID AND MINERALOCORTICOID REPLACEMENT

The pathway for making steroids in patients with CAH is typically blocked at the 21-OHP pathway. This means there is less cortisol and aldosterone produced. We can replace the aldosterone with fludrocortisone, and we can replace the cortsiol with dexamethasone (very rarely), prednisolone (quite rarely), hydrocortisone (common). The problem with this blockage is that the hormones "spill over", and you get more adrenal androgens than you would normally.

From the hypothalamus, CRF is released acting on the pituitary, producing ACTH which stimulates the adrenal glands to create cortisol. This is controlled by a thing called a negative feedback loop which is between the hypothalamus and the pituitary. It is a bit like the thermostat in your house. Think of the adrenal gland as the boiler, and the pituitary and the hypothalamus as the thermostat. If you have too much of the hormone, or too much of the heat, then the thermostat switches off. If you have too little of the hormone, or too little of the heat, then the thermostat switches on. The consequence of someone having CAH is that they have less cortisol than they would normally have.

CIRCADIAN RHYTHM OF CORTISOL

There is a big debate around how you manage patients with CAH with regards to what regime of cortisol replacement to give. The short answer is that there are not good randomised control trials to tell you what the best regime is. Therefore people prescribe steroid treatment in an individual way to achieve certain goals at certain times in life, and then other people have prejudices about how to best treat. Normally if someone does not have normal adrenal function, we give cortisol first thing in the morning to mimic the peak of cortisol. We give another dose around lunchtime to mimic the peak then, and around tea time to get the peak then. There have been places, particularly in America, where they use a reverse circadian rhythm – i.e. the high dose in the evening. There are some benefits in that, in so much that it does help to reduce the ACTH levels in the morning, and it tends to reduce the stimulus to the other hormones being made; the androgens, 17OH progesterone. But, there can be problems with that, as normally people have very low cortisol levels when they sleep. If you are taking higher doses in the evening, you have much higher steroids levels in the evening, and it is difficult for some people to sleep.

You have to balance trying to replace the hormones physiologically, with trying to suppress some of the effects of excess hormone production, and it is not as simple as merely replacing the hormone, it is also dealing with the excess androgens. There is a treatment which Prof Richard Ross has pioneered, which is not generally available, which is a long acting hydrocortisone tablet which you take in the evening. It is slow release hydrocortisone that is released overnight and through the day, which may get around some of the problems we have with people with Addison's disease and CAH, but it is not available at present.

The best way of looking at the problems we have in adults, is that the steroid treatment of CAH is the balance between two undesirable states. There is undertreatment, where we get high levels of androgens, early puberty, short stature, excessive hair growth, infertility.

If we overtreat, we get too much cortisol production – overweight, short stature, thinning of the bones, and increased risk of cardio vascular disease.

We have to walk this tightrope between these two things that we do not want. Since we do not have randomised trials to tell us what to do, then the doctor is juggling a number of factors and weighing then in order to achieve this balance. The balance that is struck depends on the things that are an issue at a given time. If obesity is a concern, people would tend to reduce the dosage to the lowest possible. If fertility is a concern, the steroid dose would be increased. We may have to play one undesirable effect against another depending on individual priorities at a given time.

MALE FERTILITY AND TARTS (TESTICULAR ADRENAL REST TUMOURS)

There are adrenal cells that are in the wrong place, i.e. around the testes. They are stimulated by high ACTH levels. If steroid therapy is increased, you can shrink them, but there is a balance with steroid therapy as mentioned before. There is a movement now to arrange ultrasounds for young men with CAH during adolescence. There is some evidence that you can shrink the adrenal rests and restore fertility via adjusting steroid doses.

MECHANISMS OF STEROID INDUCED BONE LOSS

One of the things that glucocorticoids do is to inhibit the absorption of calcium from the gut. They also increase the amount of calcium that is lost through the kidneys. As a consequence of that, there is an increase of the hormone parathyroid, and what that does is that if calcium levels are low, it tries to mobilise calcium from the bones to maintain the calcium level in the blood. So the parathyroid hormone goes up, and what that does is to increase the cells that break down the bone (osteoclasts) and you get more bone resorption. High doses of corticosteroids lower sex hormones, and that has a consequence on the bones again, further increasing resorption, leading to osteoporosis. Steroids also inhibit the cells that lay down bones, osteoblasts. (Between the osteoblasts and osteoclasts, an adult completely replaces their skeletion every 7 years).

If you give steroid doses in the physiological levels, as a replacement, we think that these are safe. In certain circumstances, particularly girls with CAH, there are high levels of androgens, and they may be protected against bone loss. So overall, people with CAH are not as severely affected with thinning of the bones as lots of other patient groups.

OSTEOPOROSIS

Patients who receive high doses of steroids may have thinner bones. Research a few years ago in Sheffield showed that male patients treated with dexamethasone have a lower bone density than those treated with prednisolone, who in turn have a lower bone density than those treated with hydrocortisone. We think hydrocortisone is the physiological treatment, which is one of the reasons why we try to use hydrocortisone as opposed to prednisolone and dexamethasone. The other thing is that weight gain tends to protect against osteoporosis. On the whole, the thinner you are, the thinner your bones are.

I have not seen osteoporosis being a significant problem in patients with CAH. I run a bone clinic every week, and I do not think it is as serious a problem as people are concerned about. I would not intervene with someone with low bone density with CAH unless they were breaking bones, as the drugs are designed for much older people. Optimising bone density can be done through steroid dosing.

There are large numbers of treatments available to increase bone mass. If you are over 40 with CAH, you can access a Fracture Risk Assessment tool online at the WHO.

CONCLUSION

Hormone replacement is a balance between two undesirable states. There are no golden rules to follow to get in right in every case. TARTs can be managed by adjustment of steroid dosage, and most people have normal fertility. With regards to bone mass, you tailor the treatment for an individual to the priorities in their life at that time.

Q&A

1. ***Do you do profiles?***

   If a patient is having problems, then we do a day blood profile, but if a patient is doing well we do not think it is necessary.

2. ***Why is it that patients get tested less and less frequently as they get older?***

   In childhood you are shooting at a moving target. In adulthood the target is fairly still, and so the changes in medication are not needed as often. The goals also change – in childhood it is around growth, weight and puberty, and so there is more intense supervision at this time in life. As they get older, the endocrinologist fades into the background, letting the patient lead a normal healthy life, and just intervening when something needs to be done.

3. ***At what age do you take children into the adult clinic?***

   That is up to the young person, and Dr Mushtaq. We tend to meet the patients in the transition clinic, and see when they would like to move over.

4. ***When should TARTs be checked for?***

   This is something that is a relatively new thing – in the past unless there were particular problems we didn't intervene. It is worth checking from around 12 onwards – but in the majority of patients these are not an issue.

5. ***What are the main issues that you come across with young women in the clinic? Any trends or themes?***

   The main concerns are around weight, hair, periods and fertility. The other factor is shorter than desired height.

6. ***Are you monitoring possibilities regarding the under absorption of medication?***

   When we do a day case, we give the tablets and monitor the levels of cortisol as well as 17OHP, and some androgens. What happens then is that you see the cortisol level going up, which indicates absorption.

SURGERY

PROFESSOR ADAM BALEN

PROFESSOR OF REPRODUCTIVE MEDICINE AND SURGERY

LEEDS TEACHING HOSPITALS

SURGERY

I've been asked to talk about surgery, and as the morning has evolved I seem to be going to talk about fertility as well, which I'm very happy to do as I'd like this to be a free-flow session.

By way of background, I am a gynaecologist with an interest in endocrinology, and I am responsible for running the assisted conception unit in Leeds. As a fertility gynaecologist, I also operate should there be surgical problems affecting fertility, and in the context of some of the disorders of the development of the internal and external female genital tract, reconstructive surgery.

We have developed what we call a multi disciplinary clinic in Leeds, and we run this clinic every other week. We see many young women with CAH right through their whole adult life with CAH. We also have very close links with the department of clinical psychology. Dr Mushtaq and I sit in on some of the transition clinics, and with Dr Orme in some of the adult clinics, and together we discuss the right time to think about reconstructive surgery. There is a big debate regarding the timing of surgery. The balance in childhood is between the cosmetic appearance, and the functional need for surgery. By this I mean that as far as function is concerned, there are no functional problems for the vast majority of young females with CAH. Even after puberty, once menstruation starts, a single opening is not usually a problem. For many years, the paediatric surgeons, historically, may have considered performing surgery in early infancy to try and make a separate opening for the vagina and the urethra. In reality, from a functional point of view, this is not really required until much later on in life.

There have certainly been many debates in the last 10 years or so, with a big shift in the way we think about managing CAH. I think this is largely due to the need to involve the individual patient in the decision making process. It may also be helpful just to go back 40 or 50 years to the way the medical profession used to view the management of some of the conditions that might have affected the development of the external genitalia. There was a view, which we now appreciate was a mistaken view, proposed by some American psychologists in the 1950's, that a child had to have a normal appearance to his/her external genitalia in order to develop as a normal individual. It was also felt at that time that non-disclosure was an appropriate way to manage families free of any worries or concerns that might then colour bringing the upbringing of a child with such problems. Now we feel that that is completely wrong, now we feel, appropriately, as I'm sure you will agree, that it is essential to involve families in all aspects of the condition that we are dealing with, and to involve you in the decision making process. When we consider reconstructive surgery, in an ideal world we should be involving the person on whom we are operating, so that they can have knowledge about what is behind that, and can discuss whether it is the right timing, and what surgery they may wish to have performed. From a functional point of view, it is not actually necessary to operate on the opening of the vagina until the young woman wishes to enter into relationships and become sexually active. It is certainly not a pre-requisite in our clinic that a young woman needs to be in a relationship before having reconstructive surgery, but we discuss with the clinical psychologist when they might wish to have surgery.

Reconstructive surgery can be simple, it can be very complicated. It may sometimes involve 2 or 3 days in hospital, it may involve 14 days in hospital. Sometimes, after reconstructive surgery, it is necessary to use vaginal dilators, which are inserted in the vagina morning and evening for 10-15 minutes in order to keep the opening of the vagina at a normal size and shape. After surgery, there will always be some scarring, which may otherwise lead to the opening starting to close up again. The young woman needs to be able to use vaginal dilators, and be comfortable using them.

The other conundrum, and big debate, is the reduction of an enlarged clitoris – is it necessary, is it appropriate, and when should it be performed? Certainly our approach has been a very hands-off approach. I certainly prefer not to perform a clitoral reduction unless absolutely necessary and if the enlarged clitoris is actually causing significant problems for the individual. There has been quite a lot of follow up studies done on women who may have had surgery in infancy, looking at the need for repeat surgery in adolescence or adult life. Most of these surveys are based on surgical practices that may have changed, as things have evolved with time, so when we look at women in their 30s, 40s, 50s, the sort of surgery they had in childhood would not necessarily be the sort of surgery that we would be performing now.

Most of the follow up surgeries have indicated that at least 50% and sometimes as many as 80-90% of women who had surgery in infancy require some sort of intervention in adult life, whether that is simply the use of vaginal dilators, but often the need for more reconstructive surgery. That is why we feel that maybe it is better to defer any surgery until development has been completed. In general terms, the first operation that we do is the operation that is likely to be the most successful. I appreciate that this is a very controversial issue, and I think you are very fortunate to have such an active society that is engaged with the medical profession to try and tease out some of these very difficult issues about appropriate management.

FERTILITY

You have heard a lot this morning about the use of steroids. That can have a knock on effect on the menstrual cycle. If there is an imbalance of hormones, the menstrual cycle may be irregular, or stop altogether. Sometimes we use the combined oral contraceptive pill to give an artificial menstrual cycle. Some forms of the pill are better at suppressing the excess hair growth that many women with CAH experience. There are also physical means, and some very effective physical means to remove excess hair. There is a topical cream called *Vaniqa* which we use quite a lot, particularly in PCOS, which has some similarities with CAH. Electrolysis, provided it is given by a trained practioner, can be very effective, as indeed can laser surgery. In the context of infertility, if a woman is having an irregular menstrual cycle, she may be ovulating irregularly, or not at all. At this point we may need to give drugs to provide regular ovulation. That can be quite a challenge for women with CAH, because the elevated 17OHP levels that we sometimes see in adult women with CAH can have a negative impact on the ability to produce eggs, and the lining of the womb as it develops. So sometimes it is necessary, as Dr Orme stated earlier, to increase the dose of corticosteroids in order to help further suppress the 17OHP and enable ovulation and fertility to occur. In rare cases, if that is a major problem, sometimes the adrenal glands have been removed completely, but that is very much a last resort scenario, and not something that is commonly required.

We have also touched upon this morning the issue of genetic counselling. Because CAH is transmitted genetically, if we have an individual with CAH, it is important to screen her partner to test whether he is a carrier of the gene, as this may colour the fertility treatment, and the management of steroid treatment in early pregnancy.

Q&A

1. ***I have a daughter who at 2 ½ months had a clitoral reduction a while ago, without a vaginaplasty at the same time. They wanting to do this now at the age of 3 and it should be a one off operation, without needing further surgery. I understood that vaginal surgery was better younger, or at puberty, due to the oestrogen levels?***

   In the transition clinics that we do, when we see young women around puberty, regardless of whether they have undergone a previous operation or not, we usually arrange an examination under anaesthetic. We do this when the individual young woman feels that this is something that she wants to have done, so that we can assess whether any surgery is required, be that repeat surgery or initial. Certainly I have seen some extraordinarily good results from surgery in infancy where repeat surgery is not required later on. The highly skilled paediatric surgeons at the moment who are operating in this field can have very good results. Having said that, because it is not required until adult life, Ii personally would suggest that surgery is not necessary until much later on. There is the British Society for Paediatric and Adolescent Gynaecology that a group of us founded 10 years ago, which has brought together not only gynaecologists, nurses and psychologists in this area, but paediatric endocrinologists, adult endocrinologists, paediatric and adult surgeons, and plastic surgeons. Our general consensus these days is to try and defer surgery. You mentioned clitoral reduction, again, that is an operation that has to be performed after careful consideration because the clitoris is an extremely sensitive organ, it is a structure that is important for sexual activity, and there is this debate as to is it important to have a cosmetically more normal appearance in childhood, or is it better to defer or even not operate at all? This is something that is highly individual and has to be discussed.

2. ***Is there an age when you should not operate?***

   I am not a paediatric surgeon, so I can't give you a straight answer to that question. If you are operating in childhood, it would normally be done by 3 or 4. I personally do not have an age, but I would prefer that they had completed puberty before undertaking surgery.

3. ***The deferments made purely on functionality and age, is there no measure on how the children are affected psychologically by that?***

   This is the research that is required now that practices have changed. There was research that has suggested that there may have been problems for some who have had surgery in infancy who then in adult life have required further reconstructive surgery, or had scarring that may have impacted their ability to enter in to relationships or enter into a normal sex life. That is where most of the research is, and that in a sense is what has coloured our practice, and also what has coloured our practice is listening to what patients tell us about their experiences. It is very difficult because surgical practices have changed – many of those who may voice problems have not had the same surgery as is done now. Our philosophy has to be to do as little as possible.

But there is no data to show that leaving a child with an enlarged clitoris isn't going to harm them psychologically through childhood?

No, and that is the issue. That is where there are a lot of clinical psychologists who are interested in this, and this is where you need their support. Sadly, in the UK, there is insufficient funding for adequate psychological services.

4. ***I have two daughters with CAH, and one without. Neither have had surgery, and had significant virilisation. At what age do I make them aware of the physical aspects?***

   That's a very good question, and I think this is where you need to be linking in with the clinical psychologist as well. My thoughts are to introduce the whole notion of how the external genitalia have been affected whilst she is young, particularly if you have a very open approach to the other aspects of it, I think it should all be discussed openly.

5. ***My child has no external vaginal opening. What are the surgical requirements to allow normal menstruation?***

   It is possible to suppress menstruation. If it is occurring and is uncomfortable, you can suppress it to defer surgery. Once menstruation starts, most growth and development has already occurred.

6. ***You say that you proceed on the patient's voice – how much of the patient's voice are people likely to hear given that the patient is going to be a young female, and in our experience all the clinicians, doctors, consultants etc have always been males, and I feel it is unlikely that young females are going to be able to confide in, or even articulate to, men.***

   That is a challenging question, since I am a male gynaecologist, and I spend my life communicating and dealing with women with a variety of medical problems, hopefully sympathetically and with empathy. We don't always get it right, but that is why I do my clinic jointly with Julie, and wouldn't have it any other way. Julie will spend time separately with our patients, as will our clinical psychologists, who are on the whole female, but not all female. We hope to be sensitive enough to be able to pick up on the concerns of the individual so that they can express what they want for themselves.

7. ***I was wondering if any of the consultants here go out to local hospitals. We don't actually live in a city, so our appointments are at our regional hospital where our consultant comes to visit. He therefore doesn't bring his nurse, or psychologist with him, so we seem to be missing out on a lot of things.***

   Ask for an appointment at a central hospital. Some of the paediatric team travel, as does Dr Mushtaq. Unfortunately it is necessary to concentrate resources in centres.

Managing CAH/DSD

Lessons from Working as a Clinical Network

PROFESSOR FAISAL AHMED

CONSULTANT PAEDIATRIC ENDOCRINOLOGIST

ROYAL HOSPITAL FOR SICK CHILDREN GLASGOW

THE NEED FOR A NETWORK

In Scotland for CAH we are looking at maybe 2 or 3 new cases per year. Since it is not very common, we need to be looking for some sort of dialogue between doctors. Another requirement for a network is that patients with complex genital anomalies (CGA) and disorders of sex development (DSD) may obtain help from multiple agencies, and one hospital may not have access to all of these resources.

The DSD Team

- Paediatric endocrinology and surgery (general, plastic, urology)
- Clinical psychology (paediatric and adult)
- Clinical genetics
- Specialist nursing
- Diagnostic imaging
- Specialist clinical biochemist
- Adult endocrinology, gynaecology, urology and surgery (general and plastic surgery), fertility services
- Forum for discussion

This is the “dream team” that one should have for looking after a child with some form of DSD.

In Scotland we have an issue with geography, in so much that we have a population that is primarily based in the central belt. Networks aim to provide the highest quality of care as close to home as possible.

Within networks it is much easier to keep ourselves educated and developed. As you have already heard from Prof Balen, attitudes and practices have changed over time, and it is very difficult for one person working in an area to keep themselves updated on what is going on, particularly in other specialities. There is a huge amount of lack of evidence with regards to what we do in clinic practice for rare conditions. It is therefore much easier to work in groups, to support each other. It also gives the children and the parents some idea that we are always thinking alike.

Working in a network requires a lot of work. I started in Glasgow in 2000, starting to develop clinics in Aberdeen and Edinburgh over the next couple of years. In 2007 we had our first meeting all together, i.e. 7 years to be able to get together and have our first meeting. Earlier than this we were having project meetings, developing newsletters etc.

Nothing gets done in medicine without the help of the government in some shape or form. We started off by asking for some research money for looking at how common genital anomalies were in Scotland. More recently, we have engaged other bodies such as the European Society of Paediatric Endocrinology to develop a research program. Just over the last year we have received some funding from the EU for further research work. The message really is that it takes a long time to get things going.

CLINICAL ACTIVITIES OF SGAN

We are there to develop patient information and education. There is multidisciplinary clinical input, e.g. ensuring that psychologists are involved as soon as possible. We would like to move to monitoring of standards in the future – we effectively define these standards in the patient information that we develop as a consensus.

The most important thing is communication. The network allows us to communicate far more effectively.

IMPROVING COMMUNICATION

We have clinics twice a year in Aberdeen and Edinburgh, and 4 a year in Glasgow. We realise that you cannot have the whole dream team at every centre, and what you need is people crossing boundaries. The network helps to avoid building a wall and prevent patients from moving around.

We also have AV links at the clinics, so you do not have to physically travel to Aberdeen from Edinburgh but can discuss things remotely.

If you want to find out more, you can go on to our website at www.sgan.nhsscotland.com

SGAN CARE PATHWAY

There are some DSD conditions that are relatively common, such as unilateral undescended testes, hypospadias, and then there are much rarer conditions such as truly ambiguous genitalia. Every clinician who deals in a given area of inpatient work such as surgery can be centrally identified in Scotland and when I started in Scotland, I could go to this office and ask for the details of every surgeon who does a particular type of surgery, which is how SGAN started off.

What we have is a SGAN Team, with named members, and the idea is that children initially come through the local SGAN team, and then come to the SGAN clinic. It is through this clinic that complex decisions will be made, and then children will go back into their local team. If specialist input such as plastic surgery is required, they would go to a specialist clinic within SGAN to see a particular clinician. Through this clinic, they do not have to stay in Scotland, they could go anywhere where we think they will get the right treatment.

In the SGAN clinic we have adult psychologists as well who come and attend. The idea is that through that clinic we can develop the whole system of transition. The gynaecologist is there from the beginning, to advise parents from the outset.

RESEARCH ACTIVITIES OF SGAN

Linked to that there are a number of research activities, some of which were actually funded by Climb CAH, such as development of the salivary testosterone analysis. There was some work done on psychosocial needs and development, where we found that a lot of parents with young children had a need for clinical psychology, but it did not necessarily relate to the extent of the severity of the problem, i.e. it was not necessarily those with ambiguous genitalia that required the support, but some of those with just hypospadias.

INTERNATIONALLY

I have talked on clinical networks. There are also research networks. I mentioned earlier that we are now being funded by the EU – what we realised over time is that whilst we were developing a clinical network in Scotland, there are also networks in Germany, Italy, etc, looking at similar issues to us.

Q&A

1. ***Are you confident as a result of this that the standard of CAH care that you would receive in Scotland would be more consistent than in England?***

   Consistent is absolutely the right word. I am still not sure if the standard of care will be the **right** standard of care, but at least we will be able to monitor it, and be consistent.

2. ***How has this development been viewed in England?***

   Prof Balen – I think this is fantastic, and we have seen what has been achieved in Scotland in other areas of healthcare as well. One of the big problems we have in Leeds is just data management – I fill in my database myself at the end of my clinic as we have no resources to update it. I think this is where Faisal has been so successful, in getting these resources.

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 Leeds conference.

Disclaimer:

Any communication from the Climb CAH Support Group is intended for informational and educational purposes only. Treatment and methods vary among hospitals and consultants, so the information quoted here may not necessarily represent the views of the Support Group, its medical advisors or other specialists across the Country. Any questions raised should be directed to your own consultant.

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