

# Deferring surgical treatment of ambiguous genitalia into adolescence in girls with 21-hydroxylase deficiency: a feasibility study.

Pierre Bougnères<sup>1</sup>, Claire Bouvattier<sup>1</sup>, Maryse Cartigny<sup>2</sup>, Lina Michala<sup>3</sup>.

<sup>1</sup>Pediatric Endocrinology, Bicêtre Hospital, Paris South University, Paris, France <sup>2</sup>Pediatric Endocrinology, Jeanne de Flandre Hospital, Lille University, Lille, France <sup>3</sup>First Department of Obstetrics and Gynaecology, University of Athens, Alexandra Hospital, Athens, Greece

## Authors' contribution.

PB made the initial decision of offering to defer surgical correction, had the first patient left unoperated and drafted the manuscript with LM. CB and MC followed the other 6 patients

## BACKGROUND

Genital surgery in Disorders of Sex Development (DSD) has been an area of debate over the past 20 years. Emerging scientific evidence in the late 1990s defied the then routine practice to surgically align genitalia to the sex of rearing, as early as possible. However, despite multitude of data showing detrimental effects to genital sensation and sexuality, few patients born with ambiguous genitalia have remained unoperated into adolescence.

## PRELIMINARY RESULTS

Preliminary results in our institution from 7 children now aged 1-8 years (median 4.5 years), suggest that it is acceptable among patients and families to defer genital operation in 21-OHD. All patients had Prader stage III or IV. Median clitoral length at birth was 24 mm (20-28 mm) and had diminished to a median of 9 mm (5-15 mm) at their last visit. Height and weight have remained strictly normal in all patients. So far girls and their parents have not expressed significant concerns regarding genital ambiguity.

	Prenatal diagnosis	Prader stage at birth	Clitoris length at birth (mm)	17OHP diagnosis (ng/ml)	T at diagnosis (ng/ml)	Age at last examination (yrs)	Clitoris length at last examination (mm)
GK	yes	3-4	25	257	8	8	15
LC	yes	3-4	20	119	9.8	7	7
LM	no	3-4	20	414	14	5.5	5
DW	yes	3-4	20	150	9	4.5	5
CL	no	3-4	25	49	14	1	10
CC	no	3-4	25	14	6.5	1	15
ON	yes	4	28	230	14.8	1	9

The ON patient treated by Maryse Cartigny

At two months of life

## OBJECTIVES

To assess the feasibility of following up non operated girls with 21-OH deficiency (21-OHD) into adolescence, so as to determine changes in genital morphology, need for surgery later in life and acceptability among patients and parents of such an approach.

## TREATMENT. ETHICS

The Saint-Vincent-de-Paul Pediatric Ethical committee granted approval for the study (2008-11). Not only parents gave their consent, but were actively taking part to the decision of deferring surgery. Girls were left unoperated following a decision from the parents and PB, CB or MC. Treatment was started at a dosage of 50 mg/m<sup>2</sup> daily in 4 divided doses, a higher dosage than usually recommended, for the 1st yr of life and 50 µg fludrocortisone twice daily. Thereafter, the daily dosage of hydrocortisone was gradually reduced to an average of 40 g/m<sup>2</sup> for the 2<sup>nd</sup> yr of life, and 10-25 mg/m<sup>2</sup> from the 3<sup>rd</sup> yr of life. We checked that serum testosterone levels remained < 0.02ng/ml.

At birth



## FEASIBILITY STUDY

The audit of the care for these 7 girls has been the incentive to formulate a research protocol to formally assess the future effects of delayed or no surgery in patients with 21-OHD.

Eligible patients will be all newborns with classical Prader III-V forms of 21-OHD referred to the DSD Rare Disease National Reference Center at the University Hospitals of Bicêtre and Lille. Parents will receive written information of the aim of the study, as well as the pros and cons of performing early surgery, based on current evidence. At this stage, and given the small anticipated number of patients taking part in the study and the nature of the intervention, randomization into early surgery or not is not considered feasible. For those patients who will require surgery, either a repeat or a first reconstruction of the vagina, this will be planned earlier in a high confluence, where the urethral sphincter lies below the confluence, so as to avoid menstrual and bladder related complications. A delayed operation will be offered to those with a lower confluence. Timing of surgery to the latter patients will depend on preference. Vaginal surgery will be performed when the girl wants to use tampons for menstruation or when she is considering becoming sexually active. Vaginal dilation will start 7-10 days postoperatively, under the guidance of the gynecological and psychology team.

Ultimate outcome measures will be adaptation, quality of life, sexual function and satisfaction in late adolescence and adulthood, using qualitative data, based on structured interviews and standardized questionnaires

