171 VARIABLE EXPRESSION OF OVARIAN FAILURE IN GALACTOSEMIA Nancy J. Hopwood, Sue E. Sauder, Inese Z. Beitins, LaVonne L. Lang, and Robert P. Kelch, Univ. of Michigan Medical School, Dept. of Pediatrics, Ann Arbor, MI USA

The pathogenesis of ovarian failure in females with classical galactosemia is incompletely understood, but is likely due to prenatal toxic effects of galactose or its metabolites on the immature ovary. We studied two sisters on dietary galactose restriction since birth who had hypergonadotropic hypogonadism. Serum prolactin and T_4 were normal and karyotypes were 46xx. AB, 17 yrs, had adrenarche at 12 yrs, thelarche at 13 yrs and menarche at 14 yrs, followed by irregular periods q 3-6 wks. BB, 16 yrs, had adrenarche at 13 yrs, but no thelarche or menarche. Bone age was 11 yrs. Pelvic U/S showed no ovarian tissue. Both girls had blood withdrawn every 10 min over 12 h (0900-2100) for pulsatile secretion of LH/FSH. BB was studied during two separate cycles: 5 and 22 days after the onset of menstrual flow. In spite of a mean intermenstrual length of 28.5 d (R 18-42 d), studies during a 6 month period in BB (pulsatile LH/FSH, weekly progesterone (P) levels, and basal body temperatures) showed no evidence of ovulation.

* x±SD	LH* mIU/ml	FSH* mIU/ml	Δ LH* mIU/ml	LH freq #/12h	E_2 pg/ml	P ng/ml
AB day 5	28.4± 6.6	5.6±1.4	15± 4	8	221	0.6
22	81.4±10.5	53.2±4.4	27±10	12	64	0.5
BB	71.4± 7.7	73.3±3.6	17± 6	11	39	0.6

These studies show that ovarian failure may be variable in similarly treated siblings. Incomplete follicular maturation most likely explains the serial observations in the least affected sibling.

172 COMBINATION THERAPY IN AN ADOLESCENT WITH POLYCYSTIC OVARIES, HIRSUTISM, TYPE A INSULIN RESISTANCE, AND ACANTHOSIS NIGRICANS. Dan C. Moore, Madigan Army Medical Center, Tacoma, USA.

A 13½ year old female presented with primary amenorrhea, weight gain and hirsutism. Examination revealed a mildly obese adolescent with a deep voice, facial and truncal hirsutism, and acanthosis nigricans in axillae and popliteal fossae. Sexual development was Tanner stage V and clitoral size 8x15 mm. The left ovary was enlarged to palpation.

Laboratory evaluation revealed a bone age of 15 years, elevation of serum testosterone and androstenedione and decrease of sex hormone binding globulin (SHBG) (Table). Pelvic ultrasound showed a cystic left ovary; laparoscopy confirmed bilateral polycystic ovaries. A glucose tolerance test showed fasting, peak and 5 hr blood glucoses of 157, 305 and 242 mg/dl, respectively, with insulin levels ranging from 144 uU/ml fasting to >400uU/ml.

			On therapy	
	Normal	At diagnosis	6 mo	2 yr
Testosterone (ug/dl)	<80	110	47	35
Androstenedione (ng/dl)	60-300	628	230	156
DHEA Sulfate (ug/dl)	60-340	156	84	
SHBG (ng bound DHT/ml)	>15	0.66	13	

The patient was placed on a combination of mestranol 50ug + norethindrone 1 mg daily and spironolactone 25 mg bid. Elevated androgen levels returned to normal and SHBG returned to near normal by 6 months of therapy and remained normal at 2 years. Facial hirsutism improved dramatically in 6 months of therapy and remains under control at 2 years.

173 A CASE OF PRIMARY OVARIAN FAILURE ASSOCIATED WITH INCONTINENTIA PIGMENTI AND MULTIPLE MINOR ANOMALIES. Hiroaki Takahashi, Kanazawa Medical University, Dept. of Ped., Kahoku-gun, Ishikawa-ken, Japan

The causes of primary ovarian failure except for Turner's syndrome are extremely rare. We have experienced a 16 5/12-year-old girl who presented with short stature (137.5 cm, -3 S.D.) and lack of secondary sexual development. Physical examination revealed immature face, typical skin changes of fading stage of incontinentia pigmenti, hemihypertrophy of extremities, ptosis of left eye lid, low set and asymmetrical ears, low posterior hair lines and atrophic nails. Bone age was 10 6/12 years. Lab data showed low estradiol (E2, 10.0pg/ml) with high FSH (139 mIU/ml) and LH (105.8 mIU/ml). FSH and LH responded excessively to LH-RH and primary ovarian failure was suspected. Chromosome analysis revealed normal 46,X X karyotype by peripheral lymphocytes and skin fibroblasts. Laparoscopic examination revealed bilateral streak ovaries and a hypoplastic uterus. IVP demonstrated no urinary abnormalities. Bilateral perceptive deafness were found and her IQ was 104. She was placed on estrogen therapy.

174 C. Thøger Nielsen, N. E. Skakkebæk, D. W. Richardson, J. A. B. Darling, W. M. Hunter, M. Jørgensen, A. Nielsen, O. Ingerslev, N. Keiding and J. Müller. University of Copenhagen, Dept. of Peds. Hvidovre Hospital and Statistical Research Unit, Copenhagen, Denmark. MRC, Reproductive Biology Unit, Edinburgh, Scotland.

SPERMARCHE (ONSET OF RELEASE OF SPERMATOZOA) IN RELATION TO SEXUAL DEVELOPMENT.

A 7-year longitudinal study of 40 normal boys, aged 8.6-11.7 years at entrance. 24-hour urine analysis for spermatozoa and testosterone was performed every three months and physical examinations every six months. The median age at spermarche was 13.4 years (range: 11.7-15.3 years). Considerable variation in secondary sexual characters was found at spermarche. The median testicular volume at spermarche was 11.5 ml (range: 4.7-19.6 ml) and the median pubic hair stage was 2.5 (range: 1-5). A pubic hair stage 1 and a testicular volume of 4.9 ml at spermarche in one boy aged 13.5 years revealed that spermatogenesis occurs in boys who may be judged clinically as preadolescents. The median age at peak velocity of urinary testosterone excretion was 13.9 years (range: 11.6-16.0 years). In most boys spermarche preceded the age at peak velocity of urinary testosterone excretion. Conclusion: Spermarche occurs early in puberty, when the phenotype is still rather infantile.

175 INFLUENCE OF AGE AND PUBERTAL STATUS ON RADIATION-INDUCED TESTICULAR DAMAGE IN THE RAT. Julian.I.Delic, S.M.Shalet, J.H.Hendry and I.D.Morris Christie Hospital,Dept.Endocrinology,Manchester,England.

Wistar rats aged 2-3 weeks (prepubertal),4-5 weeks (pubertal) or 11-12 weeks (adult) were irradiated with 300 kVp x-rays locally to the testes with doses of 1-20Gy. Estimations were made of serum LH,FSH and T and quantitative histological measurements of the testes were performed at various times afterwards. A maximum (2-4 fold) elevation in serum LH and 70% decrease in mean serum T level was seen at 8 weeks in the adult, but with restoration of normal LH and T levels by 24 weeks, indicating recovery of Leydig cell function. The younger age groups,though, exhibited early dysfunction at two weeks as indicated by reduced serum T. Although serum T recovered,serum LH became increasingly elevated with time, in the two younger groups, indicating persistent Leydig cell dysfunction. Spermatogenesis was severely disrupted in the adult rat after doses of 3Gy and above. Complete ablation of the seminiferous tubules after doses of 10-20Gy was observed, and the histological damage was associated with increased levels (1.5-2fold) of serum FSH. The younger age groups exhibited a similar threshold (3Gy) for seminiferous epithelial damage, but the damage was less severe. There was little subsequent recovery of the germinal epithelium in the adult, but this was seen in the younger groups. In conclusion, the Leydig cell of the adult is more radio resistant than that of either the pre - or pubertal rat. However the seminiferous epithelium appears to be more radio resistant in the younger rat.

176 INDUCTION OF PUBERTY BY PULSATILE LRH TREATMENT; Henriette A.Delemarre, Vrije Universiteit, department of Pediatrics, Amsterdam, The Netherlands.

11 male patients (15-24 years of age) with hypogonadotropic hypogonadism due to a central lesion are or have been treated with LRH in a pulsatile fashion intravenously. LRH was infused in 20 µg pulses in 9 and 2 µg pulses in 2 patients with a pulse interval (pi) of 90 min. In 9 of 11 pt this schedule was preceded by treatment of 4 wks with a pi of 3 hrs. In 4 patients LRH was discontinued and replaced by hCG 3000 IU im twice a week.
Results: LRH treatment with a 3 hrs pi induced a sharp increase of FSH; LH and Testosterone (T) increased slightly; testicular volume enlarged. During 90 min. pi treatment LH and T further increased; all three hormones came into adult range.
In 2 pt.started immediately on the 90 min.schedule, LH, FSH and T reached adult values directly. Virilization occurred as well as testicular growth. Until now 6 pt. had spermatozoa in the semen. 3 of 4 patients showed maintainance or even an increase of the sperm count during consecutive hCG therapy. In 1 patient with Kallmann S. spermatogenesis was not induced on LRH or hCG.
Conclusions: LRH therapy is a feasible way to obtain virilization as well as spermatogenesis in young hypogonadotropic male pt. LRH stimulation with 3 hrs pi induces an increase of especially FSH, a phenomenon present in early puberty (Burr et al. 1970). When spermatogenesis is initiated, hCG can maintain this process.

Burr et al. Pediat.Res 4:25, 1970.