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ENDOMETRIAL CARCINOMA AND HYPERPLASIA IN PATIENTS WITH GONADAL DYSGENESIS RECEIVING ESTROGEN-PROGESTERONE THERAPY. Maria D. Urban, Peter A. Lee, Claude J. Migeon, Zen Rosenwaks, Anne C. Wentz and Georgeanna S. Jones. The Johns Hopkins University School of Medicine, Department of Pediatrics and Gynecology-Obstetrics, Baltimore, Maryland.

Fifty-one patients with gonadal dysgenesis receiving estrogen-progesterone replacement therapy for periods of six months to twenty years were studied. Endometrial biopsies or dilatation and curettage were obtained in forty-seven patients. One patient on diethylstilbesterol had atypical endometrial hyperplasia which progressed to adenoepidermoid carcinoma. Six patients had benign cystic hyperplasia. Endometrial abnormalities occurred in patients with a duration of estrogen therapy greater than 3-5/12 years and who received a total lifetime estrogen dose exceeding 2500 mg of conjugated estrogen or its equivalent. Five patients who developed endometrial hyperplasia had taken cyclic estrogen-progesterone therapy; the sixth took unopposed estrogen therapy.

Total nuclear estradiol binding was measured in six patients with Turner Syndrome and nine control women. Two of the Turner patients had endometrial hyperplasia. Nuclear binding in these two subjects did not differ from that of the other patients with Turner Syndrome. Nuclear binding in the Turner patients (range 3-101/DPM ng DNA) was not different from that of nine control women at comparable stages of the menstrual cycle (34-429 DPM/ng DNA). Cytoplasmic binding of estradiol was not different in two patients with Turner Syndrome with hyperplasia from the four without.

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INTEGRATED CONCENTRATIONS OF GROWTH HORMONE (ICGH) AND GLUCOSE (ICG) IN INSULIN DEPENDENT DIABETES (IDD Robert J. Winter, Howard S. Traisman, and Orville C. Green, Northwestern University Medical School, The Children's Memorial Hospital, Department of Pediatrics, Chicago, Illinois

Growth hormone (GH) secretion was monitored continuously over 24 hours in 23 children with IDD to investigate the hypothesis that GH secretion evaluated in a physiologic fashion reflects the degree of ambiant glycemia. A constant blood withdrawal system was used on ambulatory subjects who otherwise were maintained on their usual diabetic routine.

All of the subjects studied had long standing insulin dependency and none exhibited clinical or biochemical evidence of hypoglycemia during the study period. Eight normal children (NC) were similarly studied.

Group	N	ICG*	ICGH*	r**	p value
IDD	23	291 ± 64 mg/dl	6.7 ± 3.6 ng/ml	.22	NS
NC	8	117 12	6.5 1.8	.11	NS

* mean ± 1 S.D. ** Linear regression analysis

Examination of the diurnal pattern of GH secretion revealed no difference in number of secretion episodes or in the ratio of awake/asleep GH secretion. Despite the normal mean ICGH, considerable individual variation in GH levels in IDD was observed. An additional 13 patients with IDD, not included with these data because of hypoglycemia, also had a normal mean ICGH and comparably wide individual variation.

Conclusion: There is no direct relationship between GH secretion and the degree of hyperglycemia in IDD.

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GLUCOSE INTOLERANCE IN APLASTIC ANEMIA TREATED WITH OXYMETHOLONE. Thad L. Woodard, Judith A. Wilimas, and George A. Burghen (Spon. by James N. Etteldorf), Dept. of Pediatrics, Univ. of Tennessee, and St. Jude Children's Research Hospital, Memphis, Tennessee.

The onset of glucose intolerance in three patients receiving oxymetholone for aplastic anemia (AA), an association not previously reported, led to this investigation.

Eight patients aged 9 to 20 years with acquired AA or Fanconi's anemia were evaluated. Seven had received oxymetholone at dosages of 1 to 5 mg/kg/d for 11 to 139 months and one patient did not require oxymetholone. All had oral glucose tolerance tests (OGTT) with glucose and total immunoreactive insulin (TIRI) determined at 0, ½, 1, 2, 3, and 4 hours. Seven patients had HLA analyses.

The mean glucose of the seven patients receiving oxymetholone was elevated during OGTT ($p<0.001$ for each sampling time). TIRI was elevated in five of these patients ($p<0.05$-0.001). In these five patients basal TIRI correlated with dose ($r=0.89$, $p<0.01$) and duration ($r=0.98$, $p<0.001$) of oxymetholone therapy. TIRI response areas also correlated with dose and duration of treatment ($r=0.83$, $p<0.05$ and $r=0.90$, $p<0.01$, respectively). The two remaining patients were overtly diabetic siblings with low TIRI. The patient not receiving oxymetholone had normal OGTT and TIRI levels. In one patient OGTT was normal prior to therapy but abnormal after treatment for 11 months at 2 mg/kg/d. HLA analyses revealed the siblings had a B locus antigen associated with juvenile diabetes mellitus but no other relationships were found.

These data suggest glucose intolerance is related to oxymethalone and that the mechanism may be insulin resistance.

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UNRESPONSIVENESS TO GONADOTROPIN RELEASING HORMONE (GnRH) IN GIRLS WITH UNSUSTAINED ISOSEXUAL PRECOCITY. William B. Zipf, R.P.Kelch, N.J.Hopwood, M.L.Spencer, G.E.Bacon. Univ. of Michigan, Dept. of Peds., Ann Arbor, 49109

Exaggerated or normal LH responses were reported for girls with idiopathic precocious puberty and precocious thelarche. We studied 10 girls ages $2^{9}/12$-$7^{6}/12$ with rapid breast development. During the 9 mos. to 4 yrs. of follow-up 5 girls had progressive pubertal development (group A); breast development in the other 5 (group B) either resolved or fluctuated. Two girls in group B presented with light menstrual bleeding. Clinical course could not be predicted by the initial physical exam, serum E_2 or 24h urinary estrogen excretion. The greatest E_2 value (222 pg/ml) was in a $5^{3}/12$ yr. girl in group B. Subsequent E_2 values decreased over 8 mos. to 26 pg/ml. A GnRH test (2.5µg/kg iv) was done during initial evaluation of all girls. Basal serum LH values for group A (6.6±1.6, M±SE) and B (4.1±0.6) were not significantly different; basal serum FSH values for A(10.0±2.9) were significantly greater than B(2.5±0.6). In A the GnRH response in 4 girls fell within or above the normal adult range and in one girl was normal for bone age. Three girls in B had no LH or FSH responses and 2 had low prepubertal responses. All 3 girls who failed to respond to GnRH had intermittent leukorrhea and breast enlargement and one had normal appearing ovaries on laparoscopy. One girl in B with a low prepubertal GnRH response had bilateral ovarian cysts. These observations suggest: 1) the GnRH test may be useful in predicting the clinical course of girls with isosexual precocity, and 2) autonomous ovarian estrogen production could cause isosexual precocity in some patients.

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β-LACTAMASE ACTIVITY & ANTIMICROBIAL SUSCEPTIBILITY OF HEMOPHILUS INFLUENZAE AND PARAINFLUENZAE IN MICH. D. Anderson, N. Punjabi, I. Leader & J. Hillelson (Spon. by W.B. Weil), Dept. of Human Development, Michigan State University, East Lansing, Michigan.

The incidence of β-lactamase activity of 1000 Hemophilus strains collected Sept 76-Jan 78 from pediatric and adult patients throughout Michigan (utilizing an iodometric assay, AAC 7:265:1975) was 8/52 (15%) for type b, 29/318 (9%) for non-type b H. influenzae and 31/630 (5%) for H. parainfluenzae. From Sept 76-July 77 H. influenzae type b isolates were recovered from 16 children with meningitis; none were positive for β-lactamase activity. Subsequently 4/7 CSF isolates were positive for β-lactamase activity. The in vitro susceptibilities of 30 β-lactamase (+) Hemophilus strains to ampicillin, chloramphenicol, cefamandole, cefachlor, tetracycline and trimethoprim-sulfamethoxazole were evaluated using a microtiter broth dilution method. 70% of strains were resistant to [amp] of ≥10 µg/ml (MIC range = 4-128 µg/ml), while all were inhibited by ≤1 µg/ml of chloramphenicol (MIC=0.25-1 µg/ml). Strains were highly susceptible to cefamandole (90% inhibited by ≤0.5 µg/ml), although only 25% of strains were inhibited by ≤1 µg/ml of cefachlor (MIC-1-16 µg/ml). All isolates were inhibited by [tetracycline] of ≤1 µg/ml. MICs of TMP-SMZ ranged from .0037/.148-.125/2.37 µg/ml with 75% of strains susceptible to ≤0.03/.59 µg/ml. The incidence of β-lactamase (+) Hemophilus strains in Michigan appears to be increasing. These strains are highly susceptible in vitro to chloramphenicol, cefamandole and TMP-SMZ.

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DEGREE OF INDICATION OF DRUG THERAPY IN NEONATES. Jacob V. Aranda, Ana Portuguez-Malavasi, Judi Collinge. McGill University-Montreal Children's Hosp. Depts. of Peds, Pharmacol and Therap., Montreal, CANADA.

Rational and safe use of drugs includes weighing the indication of a drug versus the risk of reactions. 110 instances of drug use were analyzed in 27 neonates with 47 identified drug reactions. Birth weight, gestational age, admission age and length of hospital stay ranged from 835-3570 g, 24-41 wks, 0.5 - 65 days, and 0.5 - 100 days respectively. To assess the accuracy of drug use the degree of indication at initiation of therapy was compared to that at discharge or completion of therapy. 9 degrees (definite, presumptive but highly indicated, resuscitative, prophylactic, procedure-related, empirical, palliative, not indicated, not classified) were based on set clinical, laboratory and pharmacologic criteria. 1/3 of drug use was definitely indicated. Of 21 drugs initially presumed highly indicated, 7 became definitely indicated, but 7 were not indicated, suggesting overtreatment in at least 30% of presumed-indicated drugs. Adverse drug reactions were noted in many drugs not definitely indicated, suggesting that risk may be greater than benefit. Data underscore the need for more careful and rational use of drugs

Indication°	Initial #(%)	Final #(%)
Definite	30 (27%)	37 (34%)
Presumptive	21 (19%)	7 (6.4%)
Prophylactic	14 (13%)	14 (13%)
Empirical	8 (7.2%)	8 (7.3%)
Not indicated	1 (0.9%)	8 (7.3%)
Others	36 (32%)	36 (32%)