facies, increased body hair, and inappropriate insulin responses to glucose and arginine. In the presence of these signs of corcoid exctiess, rapid linear growth and skeletal maturation continued in all patients. Fasting growth hormone levels and acute responses to insulin and l-arginine remained within normal limits. Urinary testosterone in the boy decreased from 15.1 μg/24 h before treatment to 1.2 μg/24 h; however, further testicular enlargement occurred during therapy.

Adrenal function in the two patients so studied revealed pituitary-adrenal suppression. Excretion of Porter-Silber (P-S) chromogens was within normal limits and not suppressed by dexamethasone. Neither patient responded to metyrapone or ACTH. Thus, it is likely that the urinary steroids measured as P-S chromogens were derived from MPA rather than from endogenous adrenal corticoids.

Experience with these patients suggests that bone advancement cannot be arrested with larger doses of MPA without producing potentially hazardous side effects.

92 *Causes of Failure of Catch-up Growth After Certain Forms of Growth Retardation.* H. David Mosier, Jr., Univ. of Calif., Irvine Coll. of Med., Dept. of Ped., Memorial Hosp. of Long Beach, Long Beach, Calif.

These experiments were carried out in order to elucidate regulation of catch-up growth and occasional failures in catch-up which are observed clinically. Growth retardation was produced in Long-Evans rats, 37 to 41 days of age, by fasting, by cortisone injections, or by propylthiouracil (PTU) feeding. The cortisone or PTU treatments were adjusted to produce maximum differences in body weight between control and experimental groups that were equivalent to the differences produced in fast periods. Light and electron microscopy of epiphyseal cartilage and tibial epiphyseal width determinations were performed in representative groups. Serial measurements of body weight and tail length were carried out for 60 to 80 days from the start of the experimental treatments. Food intake was recorded.

In the fast experiments refeeding was followed by nearly complete catch-up in body weight and tail length. After cortisone treatment there was no catch-up in body weight or tail length growth. After PTU there was a slight tendency to catch-up in body weight and tail length. The latter appeared to show a pattern of late catch-up. The results correlated with anatomic changes in cartilage.

The findings suggest that in the rat cortisone treatment in the post-weaning period permanently damages growth mechanisms and prevents growth recovery in certain circumstances. Hypothyroidism also results in a delayed catch-up in skeletal growth. These experiments illustrate certain complexities in the problem of elucidating the underlying basis of catch-up growth. The usefulness of this experimental model in studies of catch-up growth is demonstrated.

93 *The Prepubertal Androgenic Response to ACTH.* Robert L. Rosenfield, Burton J. Grossman and Natividad Ozoa. The Pritzker Sch. of Med. and LaRabida-Univ. of Chicago Inst., Dept. of Ped., Chicago, Ill.

The following studies were undertaken to explore in detail the androgenic secretory capabilities of the prepubertal adrenal. Five 6–11-year-old children with active rheumatic carditis, otherwise non-toxic, were given ACTH gel 2.2–2.9 μ/kg i.m. daily for one week as initial therapy. Plasma C 19 steroids and indices of testosterone binding protein concentration and unbound androgens were determined by competitive protein binding techniques developed in this laboratory.

Mean urinary corticoids rose from a mean (±SD) of 1.1±1.2 to 15.7±4.3 mg/day and 17-KS from 0.84± 0.69 to 3.4±0.98 mg/day. Baseline mean plasma concentrations (±SEM) were: testosterone (T) 6.7±2.4 (range 1.6±15.0), androstenedione (Δ) 15.2±4.4 (range 2.7–29.6), and dehydroepiandrosterone (D) 71.6±6.2 (range 39.8–124) ng%. Following ACTH, these were increased in each: T–22.3±3.9, Δ–149±22, and D–347±95 ng%. D-sulfate rose in each from 13.5±3.2 (range 2.3–19.8) to 62.8±24 μg%. These changes were accompanied by a fall in testosterone binding protein concentration in four. There was a concurrent rise in unbound androgen levels in all subjects as a consequence of ACTH. This steroidogenic pattern is characterized by a disproportionate increase in Δ concentration, the values sometimes exceeding those of the normal adult. Evidence, thus, has been gained that the adrenal cortex of the prepubertal child evidences a characteristic androgenic response to chronic ACTH administration.

94 *Effects of Human Growth Hormone (HGH) on 79 Hypopituitary Children.* Thomas Aceto, Jr., Alvin B. Hayles, Mary L. Parker, S. Douglas Frasier, Richard W. Munschauer and Giovanni Di Chiro, Depts. of Ped., Med., Rad., SUNY, Buffalo; Univ. of Minn., Rochester; Washington Univ., St. Louis; USC, L.A.; NIH, Bethesda, Md.

We have treated 58 idiopathic (IH) and 16 organic hypopituitary (OH) children for 12 months, using 5 treatment regimens, in order to determine optimum therapy with HGH and glucocorticoids. All patients had: growth hormone levels < 5 mμg/ml plasma during insulin induced hypoglycemia; bone ages of 12 years or less; sexual infantilism. In IH, height was –4 SD or further below the mean. In OH, pretreatment growth rate was below 2.5 cm/year. Listed are 5 treatment regimens and growth rates during therapy.

Dx	Subject No.	Age Years	HGH U; 3×/ week	Cortisone 20 mg/ M²/day	Thyroxine 0.2 mg/ M²/day
OH	10	14.9	2	+	+
OH	6	14.0	Emb. 2	+	+
IH	24	12.1	2	+	+
IH	19	11.5	2	0	0
IH	20	11.5	10	0	0

Dx	Subject No.	Age years	Growth cm/year	Failures < 5 cm/ year
OH	10	14.9	5.6±2.4	6/10
OH	6	14.0	6.8±2.0	1/6
IH	24	12.1	7.1±1.5	6/24
IH	19	11.5	9.4±0.9	1/19
IH	20	11.5	10.1±1.0	3/20

Conclusions: HGH stimulated linear growth of hypopituitary children to varying degrees; more effectively in younger smaller dwarfs, less effectively in the older

larger or cortisone treated dwarfs. HGH from embalmed bodies is clinically useful. HGH, 10 U., was not more beneficial than 2 U. The craniopharyngiomas in the OH did not grow during short-term treatment with HGH.

95 *A Longitudinal Study of Streptococcal Antibody Dynamics Showing Unusual Seasonal Fluctuations.* EDWARD L. KAPLAN, ELIA M. AYOUB, BASCOM F. ANTHONY, FRANKLIN W. BRIESE and LEWIS W. WANNAMAKER, Univ. of Minn. Med. Sch., Dept. of Ped., Minneapolis, Minn.

A population of 160 children (mean age = 6.6 years) was followed at 2-month intervals over a 2-year period with serial determinations for 3 streptococcal antibodies: antistreptolysin O (ASO), antideoxyribonuclease B (anti-DNAse B) and anti-nicotinamide-adenine-dinucleotidase (anti-NADase). Antibody dynamics of the more than 1,100 sera collected (mean no. bleedings/child = 7.3) were examined by comparing geometric mean titers (GMT) and significant rises at different times of the year. GMTs for all 3 antibodies increased during the summer and fall when streptococcal skin infections were common but leveled off or fell during the winter and spring despite a high prevalence of respiratory illnesses and positive throat cultures for group A streptococci (up to 70%). The smallest number of rises for all 3 antibodies occurred during the respiratory season. During the summer anti-DNAse B titers tended to rise more sharply and reached maximum levels sooner than the other two antibodies. Although GMTs were lowest in the 1–3-year age group, these children also showed marked rises during the summer and fall. Rises in ASO were less frequent than responses in the other two antibodies, especially after 3 years of age. Plateauing of GMTs occurred at a later age for anti-DNAse B than for the other two antibodies. This extraordinary, inverse seasonal pattern of antibody levels and responses emphasizes the predominant influence of skin infections in this population and raises the possibility of a curious immunological unresponsiveness to streptococcal respiratory infections during the winter month, behavior which may contribute to the low frequency of acute rheumatic fever relative to acute nephritis in this population.

96 *Measles in Previously Immunized Children.* STEPHEN J. LERMAN and ELI GOLD, Epidemic Intelligence Serv., Nat. Communicable Disease Center, Atlanta, Ga. and Dept. of Ped., Case Western Reserve Univ. Sch. of Med. at Cleveland Metropolitan General Hosp., Cleveland, Ohio.

An outbreak of measles (rubeola) occurred in a city in Northeast Ohio during January–June, 1969, involving 14 children previously immunized with live attenuated measles vaccine and 46 unimmunized children. In one school where the attack rate was 52.4% for unimmunized children, the attack rate for children immunized by one particular physician was 14.3% compared to 2.4% for children immunized by the local health department and other physicians. Vaccine in this physician's office was exposed to temperatures that may have contributed to virus inactivation.

This study is an example of vaccine efficacy under conditions of current community use that is less than anticipated by field trial experience. Lack of initial seroconversion is the most likely cause of these vaccine failures and deterioration of vaccine infectivity during storage is proposed as the probable explanation.

97 *Pathophysiology of* Mycoplasma pneumoniae *Infection in Human Fetal Tracheal Organ Culture.* ALBERT M. COLLIER and WALLACE A. CLYDE, Jr., Dept. of Ped., Univ. N.C. Sch. of Med., Chapel Hill, NC.

Mycoplasma pneumoniae-host cell interactions have been difficult to analyze: natural disease is limited to man, and low mortality provides little pathologic material. Data from experimental models suggest that the ciliated respiratory epithelium is the target cell of *M. pneumoniae*. Evaluation was made of fetal tracheal organ culture as a means of providing organized differentiated human epithelial cells for studies *in vitro*. Tracheas were removed from 15–20-week fetuses, obtained aseptically by hysterotomy for psychiatric indications; transverse sections were maintained in Hayflick's medium with Hepes buffer at 36 °C in 5% CO_2. The effects of *M. pneumoniae* were studied by observations of ciliary function, light microscopy and immunofluorescence. Ciliary motion (which could be quantitated stroboscopically) slowed, became disorganized and ceased by 96 h. Microscopic changes included epithelial cytoplasmic vacuolization and nuclear swelling, followed by loss of cilia. Immunofluorescence identified organisms among the cilia, between cells, and in surface microcolonies. No comparable changes were produced by 4 other human mycoplasma species which were tested. These findings suggest the pathophysiology of *M. pneumoniae* disease by revealing both functional and structural changes in parasitized human respiratory epithelium. The nature of this interaction may explain many general features of *M. pneumoniae* disease, particularly the frequency of tracheo-bronchitis with protracted paroxysmal cough which commonly occurs in childhood infections.

98 *Altered Growth Following Gestational Viral Infection of the Placental and Aplacental Host.* JOSEPH W. ST. GEME, Jr., CATHERINE W. C. DAVIS and LLOYD F. VAN PELT, UCLA Sch. of Med., Harbor Gen. Hosp., Dept. of Ped., Lab. for Microbiol. and Immunol. Research, Torrance, Calif.

Intravenous infection of 10 pregnant rhesus monkeys with mumps virus during the first trimester results in intrauterine and postnatal growth retardation. Virus may be recovered from the oropharynx of the pregnant monkey but has not been detected in the tissues of the embryo, fetus, or neonate. The maternal host develops mumps virus neutralizing antibody and delayed hypersensitivity while the infant monkey demonstrates delayed hypersensitivity alone.

Inoculation of the embryonated chick egg with mumps virus at 12 h of age results in a persistent gestational infection. At hatch virus may be recovered from the blood and organs contain virus in from 0.01 to 1.0% of their cells. Hatchling experimental and control chicks are of the same size. Within 1 week experimental chicks incur a transient growth lag which disappears by 4 weeks of age. Virus disappears from the tissues by 1 week of age. Specific antibody is present in the sera of experimental chicks at 1 month of age.

Preliminary studies reveal that parenteral mumps virus infection of the pregnant rat during early gestation results in fetal dwarfing. Virus has not been detected in late fetal tissues. Both maternal and weanling