THE STICKLER SYNDROME. Jurgen Herrmann, Thomas D. France, Jurgen W. Spranger, John M. Opitz, Univ. of Wisconsin Ctr. for Health Sciences and Med. Sch. Depts of Ped., Ophthalmol., Med. Genetics, Madison.

This paper aims to document the clinical spectrum of the Stickler syndrome and to expose the importance of making this diagnosis. Our experience is based on 43 personally examined patients from 12 families with a total of over 80 affected individuals.

The Stickler syndrome is a common autosomal dominant connective tissue dysplasia with almost complete penetrance but widely variable expressivity. Severely affected patients usually have a slender "marfanoid" body habitus, generalized muscular hypotonia, prominence and hyperextensibility of joints, and roentgenographic changes of mild (spondylo-) epiphyseal dysplasia and overtubulation. Neonatally, the "Pierre Robin Syndrome" may be a life-threatening manifestation of the Stickler syndrome. In less severely affected individuals a "flat" face and microstomia are characteristic. The major impact of the Stickler syndrome is as a cause of blindness in affected families. Moderate to severe myopia in 75% of patients is the individually most common ocular manifestation. About 20% of patients are blind due to "spontaneous" retinal detachment. It is our impression that careful follow-up and treatment of early retinal detachment may prevent some instances of blindness.

THE KQ SYNDROME. Russell O. Hess, Jurgen Herrmann. (Intr. by J.M. Opitz). Univ. of Wisconsin Ctr. for Health Sciences and Med. Sch. Dept. of Ped.

A "new" syndrome of primary skeletal abnormalities is described in 6 members of the KQ family. Genetic transmission is likely X-linked recessive but compatible with autosomal dominant inheritance with complete penetrance but less marked expressivity in females. The major clinical and roentgenographic manifestations include shortness of stature, microbrachycephaly, hypertelorism, shortness of maxilla and mandible, marked cubitus valgus, short ulnae, metacarpals and metatarsals, short AP diameter of vertebral bodies and a peculiarly straight cervical, thoracic and lumbar spine with increased lumbo-sacral angle. All the affected males are mildly mentally retarded; none have reproduced. The KQ syndrome appears to be similar to but different from the Aarskog Syndrome.

HYPOGLYCIN EFFECTS ON LEUCINE INCORPORATION INTO PROTEIN: MECHANISM FOR TERATOGENESIS? Sonja Hicks, Kay Tanaka, Francee Boches, Carol Sulis and Joseph B. Warshaw, Yale Med. Sch., Depts. of Human Genetics, Ped., Obs., and Gyn., New Haven, Conn., and Wellesley Col., Dept. Chem., Wellesley, Mass.

Hypoglycin is the agent responsible for Jamaican vomiting sickness and is teratogenic in experimental animals. Because of this teratogenic association, we investigated effects of hypoglycin on protein synthesis in vitro and in vivo. Addition of 1×10^{-5} M to 1×10^{-4} M hypoglycin to rat liver polysomal cell-free protein synthesizing systems resulted in 50 to 89% inhibition of C^{14}-leucine incorporation into acid-precipitable peptide. Hypoglycin did not effect the incorporation of C^{14}-aspartic acid or C^{14}-valine into acid precipitable peptide. To localize in vivo effects of hypoglycin, protein synthesis was measured using isolated cell-free polysomal systems obtained from livers of animals sacrificed 1 hour after the intraperitoneal administration of 15 mg/100 gm body weight of hypoglycin. Preparations obtained from hypoglycin treated animals incorporated 70% less C^{14}-leucine than controls. Combination of pH 5 enzymes from treated animals and polysomes from controls yielded only 15% of control activity suggesting that inhibition of leucine incorporation is at the tRNA level. Hypoglycin may act as a leucine analogue, competitively bind leucine-tRNA and be incorporated into protein in place of leucine.

Familial clustering of 8 minor anomalies. L.B. Holmes, Genetics Unit, Children's Service, Mass. General Hospital, Boston

We have carried out a surface examination on 5,500 newborn infants. The incidence of eight minor anomalies among the first 3,000 infants has been determined for both black (B) and white (W) newborns without major anomalies: simian crease (B 2.3%, W 3.3%), syndactyly toes 2-3 (B 0.0, W 1.1), preauricular sinus (B 1.2, W 0.7), preauricular tag (B 0.6, W 0.8), epicanthal fold (B 0.4, W 0.5), Darwinian point (B 0.1 W 1.4), Darwinian tubercle (B 0.1, W 0.5) and clinodactyly (B 4.3, W 10). Only for clinodactyly could varying degrees of severity be measured.

All mothers and about 8% of fathers were examined for minor anomalies of the hands and face. Only Darwinian tubercle was more common in the parents than in the infants. Clinodactyly and epicanthal folds were much less common in adults. The rate of recurrence of preauricular sinus and tag and simian crease among the offspring of affected parents was clearly greater than the incidence in the general population. Data on the rate of recurrence of the other anomalies is inconclusive in this sample.

The concordance rate for these 8 minor anomalies was determined for 17 sets of MZ twins and 19 sets of DZ twins. There was no significant difference, but the sample size was too small.

This study suggests racial and familial clustering of minor anomalies. A mode of inheritance may be evident when the evaluation of the total sample of 8,000 infants is completed.

INCIDENCE OF THE FETAL ALCOHOL SYNDROME IN OFFSPRING OF CHRONICALLY ALCOHOLIC WOMEN. Kenneth L. Jones, David W. Smith, Ann P. Streissguth and Ntinos C. Myrianthopoulos. Univ. of Washington Sch. of Med., Dept. of Ped., Seattle.

A pattern of altered morphogenesis and function, referred to as the Fetal Alcohol syndrome, has recently been documented in children born to mothers who were chronic alcoholics.

Records have been evaluated from the collaborative study of the National Institute of Neurologic Disease and Stroke of 23 offspring of chronic alcoholic mothers and the offspring of 2 non-alcoholic matched controls for each. For the alcoholic women, there was a perinatal mortality in their offspring of 17%, 32% of the survivors were considered to have the Fetal Alcohol syndrome and 44% had IQ's 79 and below at 7 years of age; as contrasted to a control perinatal mortality of 2%, none with indications of the Fetal Alcohol syndrome, and 9% with IQ's 79 and below at 7 years.

This frequency of adverse outcome in the offspring of alcoholic women is sufficiently high to merit serious consideration of early pregnancy termination for the chronically alcoholic woman.

CARTILAGE-HAIR HYPOPLASIA - A COMMON FORM OF DWARFISM IN FINLAND. I.I. Kaitila, E. Savilahti, P. Kuitunen and J.I. Perheentupa (Intr. by D.L. Rimoin). University of Helsinki, Children's Hospital, Helsinki, Finland and UCLA-Harbor General Hospital, Torrance, California.

McKusick first described cartilage-hair hypoplasia (CHH) as a common type of dwarfism in the Old Order Amish. We have found a high frequency of CHH (at least 30 patients in a population of 4.6 million) in Finland. In order to characterize the clinical variability of this disorder, 13 males and 15 females from 1 to 23 years of age were studied (anthropometric measurements, skeletal x-rays, gastrointestinal malabsorption tests and a variety of immunologic tests). The measurements demonstrated the severe disproportion of the dwarfism, but also revealed the presence of vertebral involvement which had been previously overlooked. Even within this homogeneous group of patients, marked variability in the degree of dwarfism, body disproportion and hair diameter was found. Two cases of mild malabsorption were found in addition to one male who had been operated upon for congenital megacolon. Earlier studies have indicated severe and even fatal immunodeficiency against viral infections in CHH. All immunological studies in these patients were normal except for constantly low lymphocyte PHA stimulation indicating a defect in cell-mediated immunity. Tuberculin skin tests were negative in 61% of the patients in spite of prior BCG. This study demonstrates the high frequency of CHH in Finland and the marked variability in the expression of this autosomal recessive disorder.