一 般 講 演 General Contribution

1. **A Case of *de novo* Rearrangements Involving Four Chromosome Nos.1,2,10 and 21: Mariko UEHARA, Mitsushiro KIDA, Hiroshi USHIJIMA, Noriko FURUMACHI** (Dept. Pediat., Teikyo Univ., Tokyo), **Akira TONOMURA and Mitsuo OSHIMURA** (Dept. Human Cytogenet., Tokyo Med. Dent. Univ., Tokyo)

An 1 year 3 months old male infant was referred to our clinic for small stature and retarded psychomotor developments. The patient was born at 2,150 g and in the 38th week of gestation with asphyxia. Because of poor sucking, he was kept in the incubation and received tube feeding for a month. At 7 months of age, he was received an anticonvalsant medication for the generalized tonic convulsion. He showed clinical findings: round face, hypertelorism, micrognathia, high arched palate, downward slanting of palpebral fissure, simian creases, hypoplasia of teeth, hypogonadism, mild limitation of abduction of hip joints. Laboratory examinations revealed 1st grade block in ECG, the irregular basic rhythm and sporadic spikes in EEG. The GI tract showed malrotation of intestine, and atrophy of brain and relative dilatation of ventricles were seen in computed tomography scanning. The karyotype of the patient was 46,XY,del(1)(q21→q25) t (1,2,10,21)(1p ter →1q21::2q 33→2q ter; 2p ter→2q 33::1q 25→1q 25→1q32::10p 15→10p ter; 10q ter→ 10p 11::21p 11→21p ter; 21q ter→21p 11::10p 11→10p 15::1q 32→1q ter). The karyotype of his mother, father and elder sister was normal.

2. **A Case of Partial Trisomy 1q: Shunsuke KIMURA, Kouji NARAHARA, Yoshifumi KODAMA and Hiroshi KIMOTO** (Dept. Pediat., Okayama Univ., Okayama)

The patient was the product of a full term gestation complicated with an early threatened abortion. Her birth weight was 2,700 g. Mother was 28 and father 35 years of age at the birth. At the age of 2 years and 5 months, she was referred to us because of poor weight gain and psychomotor retardation. Her height was 75 cm, weight 8,000 g and head circumference 47.5 cm. Physical examination revealed muscular hypotonia, hyperreflexia and a large anterior fontanelle (2×2 cm). And she exhibited multiple congenital anomalies which included elfin face in appearance with prominent occiput and forehead, malformed and low-set ears, antimongoloid slant, epicanthus, long eye brow, microstomia and micrognathia; narrow and high palate, wide-set nipples, heart murmur, long and slender fingers with flexion deformities, umbilical hernia, prominent heel and fine hair over the extremities. Dermatoglyphics was hypoplastic, showing 10 whorl patterns with extralimital triradii in the fingertips. Peripheral blood culture from the patient and her

parents were used for the chromosome analysis. G-banding studies identified the patient to have an inverted duplication at the distal end of the long arm of one chromosome 1. The karyotype was designated as 46,XX,inv dup(1q)(q32→q44) and interpreted as having the segment 1q32→1q44 present in triplicate. Karyotypes of both parents were normal. Polymorphic pattern of chromosome 1 on C-banding substantiated the abnormal chromosome of the patient to be paternal origin. Comparing the abnormal phenotype in association with partial trisomy 1q in this case to 7 previously reported cases, micrognathia, low-set or malformed ears, hirsutism, long finger or finger flexion deformities, chest deformities and large fontanelle are the most common features. However, more reports are needed in order to establish a definable pattern of anomalies for partial trisomy 1q.

3. A Case with Deletion of Short Arm of Chromosome 2 and Supernumerally Ring Chromosome: Michiko ADACHI, Hiroshi NAKAI, Hiromi OTOMO, Nobuhiro ARAI, Shigeo Hisa and Keiya TADA (Dept. Pediat., Tohoku Univ., Sendai)

A 5 month old male with 47,XY,del(2)(p21),+r is reported. He was born as the first child of healthy parents by cesarean section. His birth weight was 2,300 g. He has a peculiar face, mental and growth retardation, prominent occiput, frontal bossing, hypertrichosis on the forehead, thick eye brows, hypertelorism, ptosis, flat nasal bridge, high arched palate, funnel chest, small penis, hypotrophic scrotum, metopic suture, three fontanels, enlargement of lateral ventricles, cortical atrophy, spina bifida, retardation of bone maturation and simian crease on the left palm. Dermal ridges were hypoplastic and total ridge count was 129. Chromosomal analysis were performed on cultured lymphocytes and fibroblasts. Using G- and C-banding techniques, his karyotype was revealed to be 47,XY,del(2)(p21),+r. Under 10% of both lymphocytes and fibroblasts had lost their supernumerally ring chromosomes. In cultured fibroblasts micronucli were found in 3 cells out of 25 mitotic cells, but no bridges were observed. There may be some relation between the presence of micronucli and the loss of ring chromosomes. Clinical features were compared to the case with 46,XY,del(2)(p23) reported by Zackai *et al.* (1977), our case had some other anomalies owing to the extra ring chromosome, such as frontal bossing, hypertrichosis on the forehead, and genital anomalies. These were found in patients with trisomies of 2p, 2q, 7q, 10p, 12p, 13q proximal, and 15q. Supernumerally ring chromosome was larger than G group and had from 3 to 4 densely stained regions by G-banding technique. C-banding method indicated that the ring chromosome did not contain heterochromatic region. Moreover, no ring chromosomes were involved in satellite association. It is difficult to identify the origin of the extra small ring chromosome. But the ring chromosome was supposed to have been derived from chromosome 2, because of the clinical features and the mechanism of the breakage of short arm of chromosome 2 and ring formation in miotic process.

4. A Case of 2p Partial Trisomy Syndrome with Neuroblastoma: Hitomi NAGANO, Yuko KANO, Seiko KOBUCHI and Takashi KAJITANI (Dept. Pediat., Kawasaki Med. School, Okayama)

Thirteen cases of trisomy for the distal short arm of chromosome 2 including the present case have been reported. 2p partial trisomy syndrome presents as common features severe mental and growth retardation, a characteristic facial dysmorphism with frontal bossing and short nose with anteverted nares, abnormalities of the sternum, spine, and digits, a heart defect, and, in males, cryptorchidism and a striking genital anomaly consisting of a very small penis buried in dorsally fused scrotal skin. The patient was a boy of 8 months old born to a 25-year-old primigravida mother and a 23-year-old father, the term product of an uneventful pregnancy. Birth weight was 2,590 g. Father, paternal grandfather and uncle have cataracta and microphthalmia. At the age of eight months he was below the second standard deviation of height and weight. He had delayed motor development. He could not control his head at the age of eight months. Also noted were microcephlous, closed anterior fontanel, frontal bossing, hypertelorism, ptosis, broad flat pugnose with triangular nares, micrognathia, cataracta, microphthalmia, a midsystolic heart murmur, abdominal distension, hepatosplenomegaly, subcutaneous tumors in left axillar region, left anterior chest, and right inguinal region, a small penis buried in dorsally fused scrotal skin. He was diagnosed neuroblastoma by biopsy of subcutaneous tumor in the left axillar region. His karyotype was determined by G-banding to have a trisomy for the distal short arm of chromosome 2(2p13→2pter) resulting from the segregation of a balanced paternal translocation, t(2;16)(p13;p11). Father, paternal glandfather and uncle have balanced translocation, t(2;16)(p13;p11).

5. A Case of Chromosome 3 Duplication q Deletion p Syndrome Born to the Mother with a Pericentric Inversion, inv(3) (p25q21): Hiroko KAWASHIMA and Shigeru MARUYAMA (Dept. Pediat., Kanazawa Univ., Kanazawa)

An 18-day-old girl was referred to our hospital with cyanosis and heart murmur. She was a 1,980 g product of a 37-week uncomplicated pregnancy and the first child of healthy nonconsanguineous parents. The maternal age was 23 years and paternal age 26 at the time of the child's birth. The mother had not experienced miscarriage. There was no family history of congenital malformation and mental retardation. On admission her body weight was 2,110 g and physical examination revealed a hypotonic and cyanotic infant. Her other clinical features were as follows; hypertrichosis, frontal bossing, upward-slanting palpebral fissures, hypertelorism, epicanthal folds, long eyelashes, short and upturned nose, low-set and malformed ears, micrognathia, protruding maxilla, high arched palate, short neck, heart murmur, abdominal tumor, short extremities, clinodactyly, simian creases, camptodactyly and overlapping fingers. At age of 61 days the patient

died of heart failure. Autopsy revealed atrial septal defect, ventricular septal defect, partial polycystic kidney, eleven ribs and three lobes in the left lung. The soft and tube-like abdominal mass was left double ureters with hydropic change. G-band analysis of chromosome on cultured peripheral blood lymphocytes from the patient revealed 46,XX,rec(3), dup(q21→qter), del(p25→pter) karyotype. The mother's karyotype was 46,XX,inv(3)(p25q21). The father and maternal grandparents showed normal karyotypes. This was the first case in Japan of chromosome 3 duplication q deletion p syndrome and showed most of the clinical features described in previous 6 cases with this anomaly (Boué *et al.*, 1974; Allderdice *et al.*, 1975; Fineman *et al.*, 1978).

6. 家族性転座由来の猫泣き症候群：辻　清・西　陽造・仲野良介（和歌山医大・産婦），**上村加代子**（佼成病院）．**Cri-du-Chat Syndrome Resulting from a Familial Translocation:** Kiyoshi TSUJI, Yozo NISHI, Ryosuke NAKANO (Dept. Obst. Gynec., Wakayama Med. Coll., Wakayama) and Kayoko KAMIMURA (Kosei Hosp., Tokyo)

猫泣き症候群患児の約10%は，家族性相互転座保因者からも出生するといわれている．私たちは，1家系2家族（A, B）に猫泣き症候群患児2名を経験した．A家族では1976年10月5日，出生体重3,100 g の男児を出産，特有の子猫様泣き声，円形顔貌，低鼻，小顎症，眼裂の外下がりなどがみられ本疾患を疑い，染色体検査で 46, XY, 5p− で本疾患であることを確認した．さらに家族の染色体検査（G-バンド）を行い，患児の姉，母親および母方祖父は 46, XX (or 46, XY), t(5p−; 6q+) で，父親は正常核型であった．このA家族の染色体検査および家系図等について，本学小児科，島和子および月野隆一らが調査し，すでに第21回本学会で発表している．今回，B家族で1978年1月28日，女児（体重 2,500 g，身長 46 cm）を出生した．同様の子猫様泣き声を出す．患児は頭周囲 31 cm，顔貌は丸顔，両眼隔離，眼裂は外下がり，耳介低位，副耳もみられ，低鼻，小顎が認められる．染色体検査は 46, XX, 5p− で，本疾患を確認しえた．生下時の父年齢は30歳，母年齢は28歳で，妊娠中には特記すべきことはなかった．母親および母方祖母の染色体は 46, XX, t(5p−; 6q+) で，父親は正常である．この調査からA家族の母方祖父とB家族の母方祖母とは兄弟であることが判明した．なお，転座保因者はすべて健康である．この3世代にわたる転座染色体が2家族にみられたことにより，4世代にわたることが示唆される．このような家族性転座由来の猫泣き症候群はきわめて稀であると思われる．

7. 9番染色体過剰の細胞遺伝学的，臨床的文献考察：藤田弘子（大阪市大・生活科学）．**A Review of the Literature for Partial 9 Trisomy:** Hiroko FUJITA (Dept. Science of Living, Osaka City Univ., Osaka)

1. 臨床的考察：自験4例を含む発端者66例の9番過剰症例を臨床症状と染色体過剰部分の対応について調査した．1) pter→p21，4例の主な所見は，9p trisomy 症候群特有の顔貌と手足の末節骨形成不全，低身長，中等度発達遅滞，腕三又，b, c 欠損，猿線である．2) pter→q13，36例は1)の所見のほか骨年齢遅滞（19例）と心奇型（5例）をみる．3) pter→q31，12例はさらに関節の変形，脱臼が50%にみられる．発達は，生下時体重 2,000 g 以下8例，乳児死亡4例，3歳以上の3例では重度知能障害がある．4) q1→qter，5例は，9q トリソミー症候群の顔貌と異常に長い指（3例）が

みられる．以上の結果から，pter→p21 の過剰が 9p トリソミー症候群を起こすに充分な条件を備えていることがわかった．q 部分を含むものについて，q13 までを 9p トリソミー症候群Ⅰ型，それ以下を含むものを 9p トリソミー症候群Ⅱ型と区別することが，発達予後からみて臨床上適当ではないかと考える．p を含まない過剰は，当然 9q トリソミー症候群というべきであろう．2. 細胞遺伝学的考察：親に相互転座のある36家系の発端者核型から判断し，1) Adjacent I 11例，2) Adjacent II 6例，3) Alternate 3:1 19例の３つの segregation type に分かれる．切断点について，1)は短腕部，2)は q1 範囲，3)はq1→q31 で，過半数は q1 上である．一般的傾向と比べ，2) 3) タイプが異常に多いこと，この２つのタイプの切断点が q1 の二次狭窄部分に集中していることからみて，9 番染色体の二次狭窄には異常が起こりやすいことが示唆される．

8. 斑点状化骨を呈したトリソミー９モザイク症候群の一症例：赤塚　章・稲名市郎（大森日赤・小児），**西谷　修・北川照男**（日大・小児），**中込弥男**（国立遺伝研・人類遺伝）．**A Case of Trisomy 9 Mosaicism with Punctate Mineralization:** A. AKATSUKA, I. INANA (Dept. Pediat., Omori Red Cross Hosp., Tokyo), O. NISHIYA, T. KITAGAWA (Dept. Pediat., Nihon Univ., Tokyo) and Y. NAKAGOME (Dept. Human Genet., Nat. Inst. Genet., Mishima)

９トリソミー症候群は1973年に２例が同時に報告されて以来，モザイク例を中心に約10例の報告があるに過ぎない．私たちは，全身に多発奇形を認めるとともに，多くの関節の軟骨部分に斑点状化骨を呈したトリソミー９モザイク症候群 (46, XX/47, XX, +9) の女児例を経験したので報告する．家族歴では，母系のいとこにダウン症候群がいる．主な臨床所見としては子宮内発育遅延，精神運動発育遅延，ならびに眼球陥没，眼裂狭小，上顎突出，小顎症，耳介の変形を呈する特異な顔貌，高口蓋，股関節脱臼，右手第４・５指の亜脱臼，外性器の発育不良，ならびに肩・股・膝関節の軟骨部分，踵骨に斑点状化骨を示す骨化の異常が認められた．患者は生後 101 日目に肺炎を合併して死亡したが，心奇形は認められなかった．末梢血および皮膚の培養線維芽細胞における G バンド法による染色体分析では，モザイク率がそれぞれ26%および８%であった．その臨床症状はこれまでの報告例とほぼ一致していたが，関節の軟骨部分に Conradi 病 (chondrodystrophia calcificans congenita) に認められるのと同様な斑点状化骨を呈した点に興味があると考えられる．

9. A Case of Trisomy 9: Hideko KANAI, Masahiro ISHIKAWA, Masaki KITABAYASHI, Yoshihiro MIYAMOTO, Nobukatsu KATO (Dept. Psychiat. Neurol., Kyoto Prefec. Univ. Med., Kyoto), **Masuji MORITA and Tatsuo ABE** (Dept. Prevent. Med., Kyoto Prefec. Univ. Med., Kyoto)

The patient was a eight-year-old boy who was referred to us for generalized convulsion and mental retardation. The maternal and paternal ages in years were 26 and 31 respectively at his birth. No similar abnormalities were found in the family history. The mother was healthy and took no medications before the pregnancy. She had no serious or febrile illnesses prior to or during the pregnancy. The pregnancy was of 40 weeks duration and the birth weight was 2,200 g. At the time of delivery, he had a weakcry and was lethargic and cyanotic. At three months of age, he was diagnosed congenital

	Total cells counted	Chromosome number				
		45	45*	46	46**	47
Blood	34	2	4	3	1	24
Skin fibroblast	36	1	2	1	1	31

*, ** C-group chromosome(s) were missing.

subluxation of the hips. He walked at 18 months of age, began to speak a few words at 19 months. After having suffered from tonsillitis at four years of age, he became susceptible to febrile convulsion. At age seven, the patient had frequently nonfebrile generalized convulsions with tonic and clonic phases. Se showed dolichocephalic head, prominent occiput, a face appeared anti-mongoloid with hypertelorism, epicanthus, ptosis and strabismus, flat nose with broadened base and bulbous tip, high-arched palate, low-set and maleformed ears, small penis with bilateral cryptochidism, bilateral dislocation of hips and knees, and clubbing of webbed fingers. No cardiac murmurs were heard. Roentgenogram of heart and electrocardiogram and intravenous pyelogram were normal. The electroencephalographic findings were as follows: at rest with the eyes closed alpha waves were observed poor range and Q-waves were observed under 50 μV symmetrically. The small spikes were recorded in right central area. CT-SCAN of brain was normal. Psychologic studies revealed an I.Q. score of 73 on the Tanaka-Binet Test. Dermatoglyphic findings: simian creases were not bilateral. Digital patterns were U U U W U on the right fingers and U U U U U on the left. Total ridge count of the digits was 75.

Cytogenetic studies were performed on blood leukocytes as well as skin fibroblasts. More than 90% of examined cells showed 47,XY,+C-karyotype. Both parents showed a normal karyotype. The extra chromosome was identified as No.9 based on the G-banding method. Therefore, the patient was diagnosed as complete 9 trisomy syndrome, but the possibility of cellular mosaicism (47,XY,+9/46,XY) could not completely be discarded.

10. A Tetrasomy for the Short Arm of Chromosome 9: Kazuso IINUMA, Koji SHIMURA and Minoru HAMAZAKI (Shizuoka Children's Hosp., Shizuoka)

A female infant with a tetrasomy for the short arm of chromosome 9 identified by Q-, G- and C-banding is reported. Her main symptoms are enophthalmos, antimongoloid eye slant, hypertelorism, abnormal ears, harelip and cleft palate, hypoplasia of phalanges and nails and congenital heart defects. The girl had abnormal dermatoglyphic patterns, including clinodactyly of the fifth fingers, absent flexion crease of fingers, camptodactyly, short thumbs, fusion of subdigital triradii b and c, D line terminals in 11 on both sides and arch patterns of all digits. Chromosome analysis by peripheral leucocyte culture revealed a modal number 47 of the chromosome. The extra chromosome was a meta-

centric E16-like chromosome, which on the basis of the Q-, G- and C-banding could be identified as a dicentric chromosome of the short arm of chromosome 9 (47,XX,+dic(9)(pter→q21→pter)). The karyotypes of the parents were normal. The infant's condition deteriorated slowly, and at 62 days of age she died from acute heart failure. Necropsy revealed ventricular septum defect, patent ductus arteriosus, agenesis of corpus callosum, cerebellar hypoplasia, hydrocephaly, two lobes of the right lung, double ureters and hydronephrosis. To our knowledge, this is a third case with a +dic(9)(q21) in the literature.

11. A Partial 10p Trisomy. −46, XY, rec(10), dup p, inv(10)(p13q26)pat−: **Naoki NOMOTO** (Dept. Pediat., Kyoto City Hosp., Kyoto) **and Osamu NAGAUCHI** (Dept. Clin. Lab., Kyoto City Hosp., Kyoto)

A 9-month-old male with peculiar features and developmental retardation was reported. His clinical features included; low birth weight, dolichocephaly, widely opened fontanelles, protruding forehead, broad and pronounced cheek pouches, high and broad nasal root, broad and short nose, high arched eyebrows, horizontal eye position, slightly low set ears, large ears, thin and inverted upper lip, depressed corners of the mouth, high arched palate, retrognathia, small penis, and club feet. He had no malformation of the heart or the kidney. Computed tomography of the head revealed severe brain atrophy, moderate ventricular dilatation, subdural effusion, and hypoplasia of r-cerebellum. His weight was 6,120 g, length 66cm, head circumference 42 cm, and chest circumference 39 cm. He died of acute pyogenic meningitis on the 23 October 1978 (10-month-old). The proband was the product of a full term pregnancy born to a 26-year-old woman (gravida III, para I, spontaneous abortus I). He weighed 2,720 g at birth. All but the proband were phenotypically normal. Dermatoglyphic studies showed palmar axial triradii in the t″ position, and four whorls and one ulnar loop in digital patterns bilaterally. Using our modified Giemsa-trypsin method, karyotype was examined from peripheral blood of the proband, parents, elder brother, paternal grandfather and grandmother, and two paternal uncles. The mother, elder brother, paternal grandmother, and one of the paternal uncles had normal karyotype. The karyotype of the father, paternal grandfather, and another paternal uncle was 46,XY,inv(10)(p13q26), which showed pericentric inversion of chromosome No.10 heterozygotes. The karyotype of the proband was 46,XY,rec(10),dup p,inv(10)(p13q26)pat. He inherited one abnormal chromosome No.10 from his father and one normal chromosome No.10 from his mother. This abnormal chromosome was one recombinant chromosome in which chromosome No.10p was duplicated by crossing-over in inversion heterozygotes.

12. A Case of 12 Trisomy: Yoshio KANEDA (Dept. Pediat., Juntendo Univ., Tokyo) **and Tamiko SHINOHARA, Hisatoshi MIYATA** (Dept. Human Cytogenet., Japan Red Cross Med. Cent., Tokyo)

In this paper we report a case of 12p trisomy resulting from a familial translocation. The propositus, a male infant, was the term product of the second normal pregnancy and delivery. In the neonatal period no remarkable finding was noticed, except for anorexia. The clinical findings compared with the previous reported cases are remarkably similar with features characteristics of the 12p trisomy syndrome: peculiar flat facies with prominent cheeks; epicanthic folds; broad eyebrows; hypertelorism; broad and flat nasal bridge with short and narrow nose; large philtrum; low set ears with broad helix, prominent anthelix and deep concha; short neck; simian creases and congenital heart defect. Unfortunately no fingerprints were available. A chromosome preparation with the trypsin-Giemsa banding technique was carried out from the peripheral blood lymphocytes. It revealed that one chromosome No.11 had a prolonged short arm, with an additional band on the tip of the short arm. Further extended chromosome study on the parents showed that the mother was a carrier of a balanced translocation, 46,XX,t(11;12)(p15;p11), whereas the father had a normal male karyotype. It is obvious that the abnormal chromosome No.11 of the patient was derived from his mother. The patient is therefore trisomic for the short arm of chromosome No.12,46,XY,der(11)t(11;12)(p15;p11)mat. Maternal grandfather and elder brother also had the same balanced translocation karyotype. At the age of 10 weeks the baby died by an irreversible cardial decompensation. The most interesting autopsy finding was a complex malformation of the heart including a infantile type of coarctation of the aorta, atrial septal defect and a thick-walled left ventricle with a small cavity.

〔追加〕 **篠原多美子**（日赤医療センター・染色体）

12 trisomy の 1 例を追加する．症例は現在東邦医大小児科受診中の 9 カ月の男児．臨床症状は短頭症，hypertelorism, epicanthal folds, 低い鼻，耳介の異常，短頸，overlapping fingers などがあり，先の報告に掲げた特徴とよく一致する．染色体構成は 46, XY, 15p＋ で，両親の染色体を調べたところ，父親が No. 12 と No. 15 染色体の均衡型の相互転座をもち，したがって患児は，No. 12 染色体の短腕の trisomy と，No. 15 染色体短腕の一部の monosomy となり，karyotype は 46,XY, der(15)t(12;15)(p11;p11)pat であることが判明した．

13. Trisomy 13 Mosaicism: Suguru TANAKA, Hiroshi YOKOYAMA, Satoshi YANAGISAWA and Eitaro SUZUKI (Dept. Pediat., Yamaguchi Univ., Ube)

The patient, a female, was born to unrelated, healthy parents after 39 weeks' gestation. The mother was 27 years old and the father was 30 years old. The baby had complete cleft palate, bilateral cleft lip, depressed nasal bridge, capillary hemangioma of the eyelids, postaxial polydactyly of the left hand and both feet, rocker bottom feet, overlapping

fingers, patent ductus arteriosus, atrial septal defect, aplasia of the olfactory bulbs and nerves, and biseptate uterus. She died on 92 days of age. Repeat chromosome analyses of peripheral blood lymphocytes revealed two cell lines: 26% of the cells analyzed had a 46,XX karyotype, while the remaining 74% showed a 47,XX,+13 karyotype. Of the neutrophils from peripheral blood smears, 74% had one or more nuclear projections. Hemoglobin F level in the red cells was 55.4% at one month and 47.8% at three months. Around 9% of the patients with trisomy 13 are mosaics (Taylor *et al.*, 1970), while 2.4% of those with trisomy 21 are so. This is the second case of trisomy 13 mosaicism reported in Japan.

14. A Case of 13q Monosomy (46,XX,del(13)(q34)) Derived from Maternal Mosaicism: Tomiko MOTEGI, Yoko OZAKI and Yasuhiro ENDO (Dept. Pediat., Tokyo Univ. Branch Hosp., Tokyo), **Tetsuo IMAMURA and Noboru MOHRI** (Lab. Pathol. ditto)

A female infant with 13q monosomy who had microcephaly, a peculiar face and many other anomalies was described. The patient was the third child of healthy parents. Father was 37 years old and mother 29 at the time of birth. The first male child, who was phenotypically normal, died at 1 year 3 months old due to bronchopneumonia. The second female child was healthy and phenotypically normal. Mother had on abortion, or no stillbirth. The delivery was uneventful at 41 weeks' gestation. The attending physician noted that the placenta appeared abnormal, but the details of this abnormality could not been obtained. Birthweight was 2,740 g, length 48.5 cm and head circumference 31.5 cm. Asymmetry of the body was noted at the time of birth: the face, trunk and extremities on the left were inferior in volume to those on the right. Salient clinical manifestations were mental and somatic retardation, an usual craniofacial appearance with microcephaly, almost closing of the anterior fontanel, sloping forehead, arched eyebrows, long and straight eyelashes, upwardslanting palpebral fissures, epicanthic folds, hypertelorism, broad nasal bridge, triangular-shaped mouth, high-arched palate, micrognathia and floppy, large and cup-shaped ears, truncal hypotonia, accessory mamillae and malposition of the fourth toes, *i.e.* inferior placement, bilaterally. D.Q. at 9 months old was 22. A holosystolic heart murmur was first heard at six months old. She presented the clinical symptoms of congestive heart failure at 8 months old. Echocardiography showed a slightly paradoxical septal motion and a fluttering of posterior mitral valve leaflet suggestive of mitral prolapse. She died at ten months old due to pneumonia.

Chromosome analysis was made on cultured lymphocytes from the patient and her parents. G-bands were induced by ASG treatment. Slight asymmetry between the distal regions of the chromosomes 13 was noted in the patient when arranging the cut-out photographed chromosomes which were moderately extended, and the band, 13q34, was

absent in one of the chromosomes 13 with no evidence of its translocation to the other chromosomes. Two cell lines were observed in the mother; one normal 46,XX, the other 46,XX,del(13)(q34). The nine metaphases were confirmed as 13q34 deleted in one of the chromosome 13, when one hundred G-banded metaphases with moderately extended chromosomes out of two different 72-h lymphocyte culture were photographed to confirm the karyotype. The father showed normal male G-banded karyotype. Pathological findings at autopsy revealed segmental imperfect formation of elastica with prominent calcium deposition and edematous fibrosis of intima in the large and medium-sized arteries, and also imperfect formation of endocardial valvular elastic fibers causing mitral insufficiency. Microencephaly (brain 370 g) was observed.

15. Translocation of the Y Chromosome to an Autosome in a Phenotypically Normal Boy: Kumiko IIJIMA, Makoto HIGURASHI, Yukie IKEDA (Dept. Maternal and Child Health, Univ., Tokyo), **Kazumi IINUMA** (Shizuoka Child. Hosp., Shizuoka) **and Hiroki HOSHINA** (Dept. Pediat., Kyorin Univ., Tokyo)

In order to ascertain the frequency of chromosome aberrations among newborn infants in Japan, a chromosome survey of a large number of newborn infants is in progress at a local Medical Center located near Tokyo since 1973. In this study we have taken a way to detect the sex chromosome anomalies by using both conventional sex-chromatin method and a new banding method of quinacrine for Y-chromatin. In this short communication, one case of phenotypically normal male infant with 46,XY,−D,t (? 15:Y) was reported. This case was found during the screening studies of the 2,762 male newborn babies. This baby was born at 6th July, 1976, to a 22-year-old mother and a 24-year-old father at term without complications. The marriage was not consanguineous. The mother had had no miscarriages and the patient was their only child. His birth weight was 3,500 g and the height was 53.7 cm. The child's early development was within normal ranges. Physical measurements at 15 months of age showed his height was 81 cm and weight was 10.6 kg. At 18 months of age, his mental age was at the 18.4 months level on the Mother-Child Counseling scale and his D.Q. was 101. He could control his head at 3 months of age and started to walk without support at 12 months of age. He spoke a word at 12 months of age. Chromatin studies: X-chromatin frequency was within the male range. The frequency of double Y-chromatins was 26% from the blood smears. Chromosome analysis: Leucocytes from peripheral blood were cultured. The karyotype was 46,XY,Dp+. Q-band and C-band were done, and the segment of chromosome number 15 was the same as the Y long arm. Karyotypes of the parents were determined and the father's karyotype was the same as this patient. Mother had a normal karyotype. Laboratory findings and dermatoglyphics was within normal.

16. 18p− の2症例および 18q− の1症例：吉田洋子・藤田弘子（大阪市大・生活科学），**谷川洋子**（塚口病院）．**Two Cases with 18p− and a Case with 18q− Syndromes:** Yōko YOSHIDA, Hiroko FUJITA (Dept. Child Health, Osaka City Univ., Osaka) and Yōko TANIGAWA (Tsukaguchi Hosp., Amagasaki)

18p− 2症例と 18q− 1症例について，臨床像と染色体欠失部分の同定を行い，あわせて各症候群の発達に関して文献的考察を試みた．症例 1：46,XX,del(18)(qter→p11:) *de novo*. 6歳11カ月の女児．多量の発汗，頻回の感染症，低身長，大きな耳介，両眼隔離，鞍鼻，齲歯，翼状頸があり，発達テストでは DQ76. 症例 2：46,XY,del(18)(qter→p11:) *de novo*. 3歳1カ月の男児．低身長，筋緊張低下，眼瞼下垂，鼻根部扁平，小さな歯，翼状頸，骨発達遅延があり，発達テストでは DQ94. 染色体は 18p− のほかに 15p の肥大をみたが，Q バンドにより giant サテライトで，父由来であることが確認された．症例 3：46,XY,del(18)(pter→q21:) *de novo*. 3歳8カ月の男児．顔中央の形成不全，両眼隔離，眼振，小さな下顎，短頸，拇指の近位付着，手指の振戦，発達テストでは DQ51. ペプチダーゼAは電気泳動で両親と患児はともに Type I であったが，control および両親と比較して明らかにうすい band を示した．これは遺伝子が q21→ter の部分にあり hemizygous の状態にあることを示唆している．以上3症例の臨床像はこれまでの報告とかなりよく一致していた．発達に関しては，文献より 18p− の10人（前脳症を伴う者はいない）の IQ は50～75で，平均 IQ 63，18q− の7人の IQ は37～59で，平均 IQ 51 であった．両症候群とも精神発達遅滞は比較的軽度であり，今回報告した症例2は正常範囲であるが，現在3歳であり，今後追跡を行いたいと考えている．

17. 端部着糸型染色体の短腕を含む転座における切断点の同定：石井ふみ代・平野康子・藤田弘子（大阪市大・生活科学），**松尾和子**（大阪市立十三市民病院）．**Break Point in Short Arm of Acrocentric Chromosomes Involved Translocation:** Fumiyo ISHII, Yasuko HIRANO, Hiroko FUJITA (Dept. Child Health, Osaka City Univ., Osaka) and Kazuko MATSUO (Osaka Municipal Juso Hosp., Osaka)

端部着糸型染色体の短腕を含む相互転座とロバートソン転座について多くの報告がある．しかし，転座染色体に仁形成部や付随体が存在するかどうかについての報告はまだ少ない．われわれは G-分染法によって確認した相互転座2例とロバートソン転座3例について，C-，Ag-，Q-染色法を施し，端部着糸型染色体の短腕部における切断点の同定を行い，とくに仁形成部の存在を調べた．その結果，相互転座・46,XY, t (7;15)(7pter→7q22;15qter→15p13::7q22→7qter) と，46,XY, t (15;20)(15qter→15p13::20cen→20pter;20qter→20cen) には仁形成部の存在があった．Q-染色で，付随体は陰性であった．ロバートソン転座・46,XY,−14+tdic(14;21)(14qter→14p12::21p12→21qter), 46,XY, −21+t(21;21)(21qter→cen→21qter),46, XX,−21+t(21q21q) では3例とも仁形成部の存在は認められなかった．Ag 染色を用いて仁形成部の存在を調べた報告は，少なくとも相互転座は5例，ロバートソン転座の4例が発表されている．今回の結果を含めると，相互転座では端部着糸型染色体において，仁形成部の遠位で切断されているものは4例であった．あと2例は仁形成部の近位で，残り1例は仁形成部の中央で切断されているが，仁形成体と付随体部は消失されることなく相手染色体の切断部に転座している．しかし，ロバートソン転座では，仁形成部の存在を認めた報告はなく，仁形成部は活動していないか，あるいは欠失したものと考えられる．

18. A Case of Typical Down's Syndrome with mos 46,XX/46,XX,−21,+i(21q): **Hiroshi NAKAI, Michiko ADACHI, Morikuni FUKUDA and Keiya TADA** (Dept. Pediat., Tohoku Univ., Sendai)

Down's syndrome is one of the most popular chromosomal aberration syndrome, but a translocation-typed mosaic Down's syndrome is very rare and it is important to consider how such aberration had been appeared and to know the difference of phenotype according to the mosaic ratio. A new case of Down's syndrome with mos 46,XX/46,XX,−21,+i (21q) was a product of a gravida 3, para 0, abortus 0, mother of 27 years old and a father of 32 at her birth. Her birth weight was 2,700 g. Physical examination of the patient showed flat occiput, hypertelorism, epicanthus, flat and broad nasal bridge, malformed and low set ears, anteverted nostrils, macroglossia, simian crease on the left palm, and clinodactylies of the Vth fingers. She could not control her head nor sit down at her 6 months of age. Dermatoglyphic findings were eight ulnar loops and two whorls on the finger tips, the III interdigital distal loop patterns, highly positioned axial triradius, and tibial arches on the bilateral hallucal areas. Cytogenetic studies, using G banding technique, revealed the patient's karyotype as mos 46,XX/46,XX,−21,+i(21q), and the mosaic ratio (1:4) showed an advantage of aberrant cell line. From the distribution of chromosomes 21 with giant satellite in the normal and aberrant cell lines, it was suggested that the isochromosome formation might have been occurred in zygotic cleavage on early stage after fertilization.

19. A Case of Trisomy for the Proximal Segment of the Long Arm of Chromosome 21: **Etsuji OKAMOTO, Miyoko KOHNO and Koso OHAMA** (Dept. Obst. Gynec., Hiroshima Univ., Hiroshima)

A 3-year-7-month-old girl with partial trisomy 21 (pter→q21:) was presented. The patient was born after 39 weeks of gestation to a gravida 4 para 3, 44-year-old mother and a 34-year-old father. The family history showed nothing to be mentioned. Course of her pregnancy was uneventful and her birth weight was 2,600 g. Since 2 months of age, she was suffering from reccurrent attacks of pneumonia. At 5 months of age, she was pointed out VSD and made a diagnosis of Down's syndrome because of the presence of the following findings; dry skin, hypotonic muscle, saddle nose, bilateral simian creases, right short fifth finger and distal loop in the third interdigital areas bilaterally. Her mental development was retarded, particularly in speaking. She also showed slightly retarded physical development; at 3 years and 7 months of age, weight was 12 kg and height was 85.5 cm. Superoxide dismutase-1 of which gene locus is seemed to be located on the distal portion of the long arm of chromosome 21 (21q22) was analyzed in this case and showed normal activity, 10,741 unit/gHb. Chromosome analysis of the patient was performed

from peripheral blood lymphocytes with trypsin G-banding technique. All the cells analyzed had 47 chromosomes with a small acrocentric chromosome, which was ascertained as a chromosome 21 deleted at the portion of band q21. The karyotype could be designated as 47,XX,+del(21)(pter→q21:). The chromosomes of the parents were apparently normal. There are several reports on the determinant portion of chromosome 21 for the Down's syndrome phenotype. It is generally considered that the Down's phenotype is due to the trisomy of the distal portion of the long arm of chromosome 21, probably the portion of q22 (Aula *et al.*, 1973; Williams *et al.*, 1975; Hegemeijer and Smit, 1977; Cervenko *et al.*, 1977; Ballantyne *et al.*, 1977). The present case may provide a valuable information on the relationship between the genes located on the long arm of chromosome 21 and the expression of Down's phenotype.

20. A Case of Partial Tetrasomy 22: Hiroko YAMAMOTO, Yoshiaki YAMAMOTO, Tsuneo TSURUHARA, Toshiaki OURA (Osaka Child. Med. Center, Osaka) **and Hiroko FUJITA** (Osaka City Univ., Osaka)

A case of partial tetrasomy 22 was reported. This male infant was born after uncomplicated 41 weeks gestation. His parents, both 28 years old, were healthy and unrelated. Family history was unremarkable. Delivery was normal and birth weight 3,430 g. He took formula poorly and gavage feeding was introduced during first two days of life. On physical examination, odd looking face with hypertelorism, antimongoloid slant of the palpebral fissures and epicanthal folds, depressed nasal bridge, micrognathia, large malformed auricles and preauricular skin tags was noted. Left inguinal hernia and cryptorchidism were also noticed. Physical growth and psychomotor development were nearly normal. He walked at 16 months and developmental quotient at the age of 10 months was 88. Chromosomal study of peripheral lymphocytes revealed 47,XY with an extra small metacentric chromosome, which seemed identical to a partially deleted chromosome 22 by G- and C-banding. By more detailed examination, however, this extra chromosome was noted to have satellites on both ends of the arms. Satellite association with D or G group chromosomes was also found. Furthermore, Ag-banding method demonstrated satellite stalks on both arms. According to these findings, the abnormal extra chromosome was identified as isochromosome for short arm of No.22. He thus had the karyotype of 47,XY,i(22p). The karyotypes of his parents were normal. In previously reported cases of partial trisomy 22, clinical features are as follows: mental retardation, congenital heart disease, and certain facial characteristics including antimongoloid slant of the eyes, low set or deformed ears and preauricular skin tags or sinuses. In addition to these findings, cleft palate and skeletal anomalies are frequently present in cases of full trisomy 22. The facial appearance of our patient shows a striking resemblance to that

of reported cases. It is remarkable that visceral anomalies are minimal and psychomotor development is nearly normal in this patient of partial tetrasomy 22.

21. A Case of Partial Trisomy 22 Resulting from a Familial 11/22 Translocation: **Kouji NARAHARA, Hiroshi KIMOTO** (Dept. Pediat., Okayama Univ., Okayama), **Motoji KAMOI, Teruyo TANAKA and Hideo INOUE** (Dept. Pediat., Okayama Saiseikai Sougou Hosp., Okayama)

A female infant with multiple congenital malformations identified as partial trisomy 22 was presented. The proband was born at term to a 25-year-old gravida 5, para 2, abortio 3 mother and a 30-year-old father. The mother, father and an older female sib were phenotypically normal. The body weight at birth was 2,600 g, height 47.0 cm and head circumference 32.0 cm. Shortly after birth the infant exhibited few spontaneous movements, which were probably the result of neonatal asphyxia (Apgar score 7), but no hypotonia. Examination at one month of age revealed following abnormalities; microcephaly, micrognathia, cleft palate, large low-set ears, bilateral preauricular sinuses and skin tags, ptosis of both eyelids, short palpebral fissures with a mongoloid slant, long philtrum, cardiac murmur, long and slender fingers, and limitation of abduction of the hip joints. The proband had shown gross psychomotor and growth retardation in the succeeding months, and died suddenly of an illness with high fever and convulsion at 8 months of age. Autopsy revealed atrial septal defect but no abnormalities in other organs. Chromosome analysis of the proband demonstrated an extra small acrocentric chromosome. On G- and R-banding, karyotype of the mother showed a translocation between No.11 and No.22 chromosomes (46,XX,t(11;22)(q25;q13)). Hence karyotype of the proband was identified as 47,XX,+der(22),t(11;22)(q25;q13)mat. It appeared very likely that aneuploidy of the proband had occurred as a result of 3 to 1 segregation during the meiosis I of the mother. Comparison of clinical features between the 11 reported cases of partial trisomy 22 for the part from pter to q12 or proximal q13 and the 22 cases of full trisomy 22, either of which had been identified by banding techniques, was carried out. Mental and growth retardation, preauricular sinuses and skin tags, large low-set ears, congenital heart disease, antimongoloid slant of palpebral fissures, cleft palate and skeletal anomalies were common clinical features. On the other hand, typical craniofacial features noted in the cases of full trisomy 22 including microcephaly, long beaked nose, long philtrum and marked micrognathia were less prominent in the cases of partial trisomy 22. These findings suggest that trisomy for the part from pter to q12 or proximal q13 is responsible for most clinical features of the trisomy 22 syndrome.

22. **Two Cases of Trisomy 22 with Auditory Disturbance: Takashi KATANO,** (Hiroshima City Welfare Ctr. for Handicapped Child., Hiroshima), **Hideki YAMAOKA, Takashi TAKIGUCHI, Akihiro SHIOTE, Motochiyo MURAKAMI** (Hiroshima City Hosp., Hiroshima) **and Tetsuji KADOTANI** (Kadotani Med. Res. Found., Higashi-hiroshima)

On the basis of G- and Q-banding techniques, two cases of trisomy 22 were detected, which were trisomy 47,XY,+22 and partial trisomy 47,XY,+22q−(q13). The clinical features of these two cases were compared as follows: the congenital heart failure was total anomalous pulmonary venous return (TAPVR) in the +22 and atrial septal defect (ASD) in the +22q−, mental retardation of the +22 was severe than the +22q−, developmental retardation was higher in the +22 (6.9 kg) than the +22q− (7.8 kg) at two-years-old, the examination of auditory brain stem response (BSR) was −85db in the +22 and −70db in the +22q−, the facial features were mild in the partial trisomy 22. The more detail was reported in *Proc. Japan Acad.* **54**, (B), 163–166 and *ibid*, 217–221.

23. **A Case of 46,XXq− with Turner Stigmata and Diabetes Mellitus: Noriko NAKATA, Kazuyuki ISHITOBI, Akira WATANABE, Takako KATSUTA and Yoshimichi HARADA** (Dept. Med., Tottori Univ., Yonago)

A woman born April 1, 1946, was first admitted to our hospital in 1970, for evaluation of primary amenorrhea, short stature, and diabetes mellitus. The mother was 31 and the father 37 years of ages when she was born. There was no consanguinity. She was the 4th of 4 children. All siblings and her mother were healthy. The father was died of dysentery before her birth. There was no family history of short stature or diabetes. The delivery was unremarkable and her birth-weight was 2.5 kg. At the age of 5 years, she was noted to be shorter than her peers. Her growth and development were retarded. Mental development and school performance was normal. She failed to develop secondary sex characteristics at the usual age of puberty and never had a menstrual period. Polydipsia, polyuria and visual disturbance started at the age of 22. At 24 years of age, she weighed 27 kg and was 136 cm tall. She looked old for her age, and had loss of scalp hair. She did not have webbed neck, low nuchal hairline, short metacarpals, or hypoplastic nails. Cubitus valgus was present. The nipples were widely spaced and there was no breast development. Pubic hair was scanty and axillary hair not. The external genitalia were infantile. She showed more pigmented naevi than her mother. Urinary sugar excretion was 30–70 g/day. Fasting blood sugar was 177 mg/dl, and blood sugar curves after oral glucose loading showed diabetic pattern. Thyroid and adrenal function tests were normal. Basal serum LH was 118 mIU/ml, FSH 240 mIU/ml. These values increased higher than 500 mIU/ml after an injection of 200 μg of LH-RH. X-ray examination showed the flattening of the tibial heads with deformities of the medial tibial condyles. Epiphyseal

lines were closed. X-ray of the pelvis revealed dislocation of the left hip joint. In dermatoglyphics, the total finger ridge count was 177 and simian crease was present on each hand. Buccal smears showed sex chromatin in only 2.3% of the cells. The drumstick in polymorphonuclear leucocytes was present in 1.7%. Mean ratio in size of drumstick to nuclei was 1.5%. Peripheral blood leucocytes were cultured, and 65 metaphases were examined. The modal number of chromosomes was 46. Karyotype analysis revealed a missing chromosome in the C group and an extra submetacentric chromosome similar to the No.16. No cells consistent with 45,X were observed. Autoradiographic study showed one of the 3 chromosomes in the No.16 group was found to be uniformly and heavily labelled, suggestive of its being the partially deleted X chromosome. The breakpoint was at q21, the karyotype being 46,X, del(X)(pter−q21) by the banding methods. These findings and their relation to clinical features and phenotypic-karyotypic correlations in the other reported 15 cases with 46,XXq− and 13 with 46,XXp− were discussed.

24. ターナー症候群の追跡的観察による身体発育の特徴： **池田由紀江**（筑波大・心身障害），**日暮 真・飯島久美子**（東大・医・母子保健），**保科弘毅**（杏林大・小児），**石川憲彦・大関武彦・江木晋三**（東大・小児）． **Anthropometric Measurements of Children with Turner's Syndrome:** Yukie IKEDA (Univ. Tsukuba, Ibaraki), Makoto HIGURASHI, Kumiko IIJIMA (Univ. Tokyo, Tokyo), Hirotake HOSHINA (Kyorin Univ., Tokyo), Norihiko ISHIKAWA, Takehiko OHZEKI and Shinzō EGI (Dept. Pediat., Tokyo Univ., Tokyo)

10例の Turner 症候群 (45,X 4例, 45,X/46,XX 4例, 45,X/46,XXq−/46,XX 1例, 46,XXqi/46,XX 1例) について人類学的計測を縦断的に実施した．計測開始年齢は8カ月～14歳の範囲にあり，計測回数は1～11回の範囲のべ27回であった．計測方法は，マルチン式人体計測器にて藤田の方法である．対照群として木田 (1957)，岡田 (1972)，池田 (1977) の値と比較した．各計測の値を各症例の年齢に相応した対照群の平均値からどの程度偏っているかを standard score であらわして比較した．Turner 症候群では身長，下肢長，上肢長が著しく小さく，したがって身長に対する比下肢長，比上肢長が小さかった．これに対して胸部の発育は良く，胸囲，胸部矢状径は対照群の positive side にあり，胸部横径も対照群のほぼ ±1 SD にあった．手，足では幅は正常範囲であるのに対し長さが小であるため，手示数，足示数は positive に偏っていた．また，骨盤幅，肩峰幅は対照群の ±1 SD の範囲にあった．最大頭長，最大頭幅，頭囲は変動が大きく一定の傾向は明らかでなかった．頬骨弓幅，内眼角距離，形態的顔面高では対照群の ±1 SD にあった．

25. Karyotypical Mosaicism in Turner's Syndrome: **Kunikazu KISHI and Akira TONOMURA** (Dept. Cytogenet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

Turner's syndrome with 45,X is one of the most encountered chromosome anomalies in spontaneous abortions, whereas it is very rare in newborns being only 0.01%. This may suggest that the vast majority of 45,X conceptions do not survive and those which

survive to term are mosaics. However, a number of literatures show that more than half of patients with Turner's syndrome clinically examined are to be 45,X. In order to clarify this conflicting figure, it is necessary to analyse whether they are to be 45,X or to be mosaics in more detail. In this study, mosaicisms of 47 patients were examined after analysing 100 metaphases of lymphocytes cultured for 50 hr. When the patients had been determined to have a single cell line of 45,X, chromosomes of fibroblastic cells were examined. Results are as follows: 2 cases had 45,X (4.3%), 4 cases were 45,X/46,XX (8.5%), 7 cases were 46,X,i(Xq) (14.9%), 20 cases were 45,X/46,X,i(Xq) (42.6%), 9 cases were 45,X/46,X,r(X) (19.1%) and 5 cases were others (10.6%). The frequency of 45,X was very low compared with that of the previous reports. Causal relationship between the number of centromeric heterochromatin and mosaicism was also investigated for patients with 46,X,i(Xq), because mitotic disturbance of dicentric chromosomes will form 45,X cells and lead to mosaicisms. Using C-banding technique, iso-X chromosomes were classified into two types; i(Xq) and dic(X)(p11). The former showed a single centromeric heterochromatin and the latter had two. There were 3 cases of 46,X,i,(Xq) (13.6%), 5 cases of 45,X/46,X,i(Xq) (22.7%), 3 cases of 46,X,dic(X) (13.6%) and 11 cases of 45,X/46,X,dic (X) (50.0%) among 22 cases examined. The higher frequency of mosaics was found in patients with dic(X) than in those with i(Xq), but it was not significant.

26. Unusual X Chromosome Anomaly: 45,X/46,X,t(X;X)(q_{26};q_{26}) and Systemic Lupus Erythematosus in a Woman with Gonadal Dysgenesis: Shunro ITANI (Int. Med., Kyoto Hosp., Japan Tobacco & Salt Public Corp., Kyoto) **and Takashi HOSHINO** (Dept. Int. Med., Kyoto Univ., Kyoto)

A 20-year-old woman with primary amenorrhea and a few Turner's stigmata who initiated systemic lupus erythematosus (SLE) at age of 19 was studied. Such abnormal dermatoglyphics as high total finger ridge count and variant palmar creases were observed. Her chromosome constitution showed a mosaic of 45,X/46,XXq+. The abnormal chromosome formed a large X chromatin body, late DNA replicating pattern and two symmetrical C bands. G banding techniques revealed that the chromosome consisted of two X chromosomes attached long arm to long arm forming an X-X translocation and was identified as t(X;X)(q_{26};q_{26}). There are increasing evidence indicating the relation between X chromosome anomaly and autoimmune disorders. It was suggested that the association of an unusual X chromosome anomaly with SLE in the present patient would be not merely fortuitous but support this concept.

27. **Dicentric Y Chromosome and Sexual Differentiation: Jun-ichi FURUYAMA, Noriyuki SUEHARA** (Dept. Genet., Hyogo Coll. Med., Nishinomiya), **Takezo SHIN** (Dept. Urol., Osaka Pref. Hosp., Osaka), **Tokiko OOGAME** (Osaka Ketsusei Inst., Osaka) **and Masaaki TATO** (Suita Hosp., Osaka)

The role of the genes on Y chromosome was discussed through the survey of the cases with dicentric Y including our patient. The patient was 29-year-old male. He had short stature, low weight and small penis from the time of his childhood. His intelligence and character were normal. He noticed the growing abdominal tumor and visited the hospital. He had gynecomastia, small penis with hypospadia. His left testis was small but the right was 15×16 cm. The axillary and pubic hair was scanty. His right testis was rejected and showed seminoma. Cytogenetic examination carried out on peripheral blood demonstrated two cell lines, the one being 45,X and the other 46,X,dic(Yq). They were in the ratio 1:4. Endocrinological study could not be done because of his death. Since the first case of X/X,dic(Yq) was reported by Yunis in 1965, approximately twenty patients have been observed till now. The phenotypic presentations were diverse from male to female. This variation may be caused by whether existence or missing of the genes controlling the development of the testis in the formation of dicentric Y, and may depend on the existence of X/X,dic(Yq) mosaic cell population as the X cell line causes an incomplete gonadal differentiation. We are observing an another patient bearing probably a small Y chromosome formed by the region near the centromere. The external genitalia were male and the penis was small with hypospadia. If a small Y chromosome of the patient include the genes controlling the testicular differentiation, his genitalia should be developed normally. This observation implies that another gene in the distal region of Y chromosome is essential to develope into the normal male.

28. **A Case of Isochromosome for Long Arm of Y: Yoshiaki YAMAMOTO, Susumu NAGAHARA, Hiroko YAMAMOTO, Tsuneo TSURUHARA** (Osaka Child. Med. Center, Osaka) **and Hiroko FUJITA** (Osaka City Univ., Osaka)

A superficially female infant was investigated for abnormal external genitalia and left inguinal hernia at the age of one month. Her parents are unrelated and have acquired hearing defect secondary to febrile illness. Her mother and maternal grandparents were noted to have inguinal hernia, but no other anomary was found in the family. Her mother's first pregnancy was terminated by induced abortion one year before her delivery. The pregnancy was uncomplicated and delivery was uneventful. Gestational age was 41 weeks, birth weight 3,000 g, length 47.5 cm, head circumference 32 cm, and chest circumference 31.5 cm. Her external genitalia was female type with enlarged clitoris and a large inguinal hernia was noted on the left side. Vagina was visualised on cystourethrography. Chro-

mosomal examination of 100 peripheral lymphocytes revealed two cell lines; 80 cells had 45X chromosomal constitution, and 20 cells had 46 chromosomes with one dicentric chromosome. This abnormal chromosome was as large as No.16, and the cell was negative for X chromatin and positive for Y chromatin staining. G-banding showed symmetrical bands on both arms. In the C-banded preparations, heterochromatin, which is usually noted on the long arm of Y, was found at the end of both arms. This heterochromatin was more prominent in the Q-banded preparations, and these findings indicated that this abnormal chromosome was isochromosome for long arm of Y. Thus, her karyotype was 45XO/46Xi(Yq). Testosterone response to gonadotropin stimulation was as high as normal male infant. Estrogen showed no remarkable elevation. Plasma HGH, TSH, LH and FSH were normal. Af five months, bilateral hernioplasty and left gonadal biopsy was performed. On operation, Fallopian tubes were found on both sides, but right gonad could not be examined. Histological examination of the left gonad showed atrophic testicular tissue. Investigation of previously reported cases of isoYq revealed that internal and external genitalias were almost exclusively female appearance. Whereas, gonadal findings showed striking variations such as undifferentiated testis, ovotestis, or streak gonads. It is speculated that physical male determining factors are located in the short arm of the Y chromosome. In 16 of 19 reported cases, the karyotypes were mosaics with 45XO.

29. 46,XYq− の1症例：Yq ヘテロクロマチンの意義について考察： **山田清美・長谷川知子・岩動孝一郎** (国立病院医療センター，遺伝・泌尿器)． **A Case of 46, XYq− with Special Consideration on the Phenotypic Effects of Yq Heterochromatin:** Kiyomi YAMADA, Tomoko HASEGAWA and Koichiro ISURUGI (Div. Genet. and Dept. Urol., Nat. Med. Cent. Hosp., Tokyo)

異質染色質が一部分欠失したY染色体をもつ個体を発見したが，臨床症状および検査所見から類宦官症と診断されたので，この症例を詳細に報告するとともに，これまで遺伝的な活性をもたないとされている Yq 異質染色質の表現型に及ぼす影響について考察を加えた．症例：21歳の大学生．性器発育不良を訴え，精密検査を希望して当医療センター泌尿器科で受診．17～19歳の2年間岡山大学病院泌尿器科にてホルモン治療を受けていた．身体所見では，陰茎矮小（小指等大），左右の睾丸も矮小，女性様乳房を認める．身長は 161 cm と低いが，両親とも身長は低いほうであった（父 161 cm，母 155 cm)．ホルモン検査では，血中テストステロンの異常低値 (63.5 ng/dl) と血中 FSH の異常高値 (929.3 ng/dl) を認める．hCG 負荷テストにおける血中テストステロンの上昇反応は良好であった．睾丸組織は，低精子形成を示しており，精原細胞は散見されるが成熟精子は極少であった．細胞遺伝学的研究：患者のリンパ球・睾丸組織・皮膚組織由来の培養細胞の核型は，いずれも 46,XY．末梢血塗沫細胞は Y-クロマチン陰性．父親のY染色体の長さと比較して，del(Y)(q12) と断定された．21q の長さを基準にすると，父親の Yq の長さの平均値は 1.53 (n=100)，患者は 1.12 (n=35) で，父親の Yq 異質染色質 (Yq12) の約65%の欠失と判定された．考察：これまでの正常男性における調査から，Yq が1.14以下の男性は267人中で10人発見されている．本症例の解釈として，Yq の欠失が表現

型に影響を与えたのではなく，偶然に類官宦症の患者にみられたのであって，両者の因果関係はないとする見解もある．しかし，演者らは Yq 異質染色質を全くもたない正常男性の存在が不確実であることと考え併わせて，Yq 異質染色質の明らかな欠失による場合には精子形成能に影響を与えるのではないかという考えを述べた．

30. A Cytogenetic Survey of an Institution for the Mentally Retarded Patients: Ikuko KONDO, Hideo HAMAGUCHI, Michiko YAMADA (Dept. Human Genet., Univ. Tsukuba, Ibaraki) **and Tadashi HANEDA** (Dept. Psychol., Ibaraki Pref. Hosp., Mito)

A cytogenetic survey was carried out for 449 patients, consisted of 261 males and 188 females, in an institution for mentally retarded patients. The population ranged in age from 6 to 66 years old, and 324 patients were adults. I.Q. of most of the patients (93%) were under 51. In total 37 patients (8.1%) were shown to have chromosome abnormalities. There were 33 individuals with Down's syndrome, and all of them had been recognized clinically. The sex ratio of the patients with Down's syndrome was 2.3, which was similar to those in other studies. In addition, we found one patient with 46,XY/47,XY, +12p, one with 46,XY,r(22), and one with 45,XY,−13,−14,+t(13q;14q). Only one female, who was moderately retarded, was found to have an abnormal sex chromosome constitution, 47,XXX. The proportion of chromosome abnormalities in the etiology of mental retardation in the present survey is highly significant, and most of the patients with chromosome abnormalities were Down's syndrome. Similar findings were also reported by Jacobs *et al.* (1978). Result of this survey indicates that it may become more important problem how to manage the patients with Down's syndrome, with advance of the medical and social welfare for mental retarded patients.

31. The Frequency of Chromosomal Aberrations in the Severely Mentally and Physically Retarded: Hitoshi KANEKO, Kazuo HOSHINO, Hirotada TAKASHIMA (Ashikaga Nat. Hosp., Tochigi), **Tokihiko SEKIGUCHI** (Seiransoh Nat. Hosp., Ibaraki) **and Kazuo BABA** (Dept. Pediat., Nihon Univ., Tokyo)

Usually, the frequency of chromosomal aberrations in newborn babies is estimated about 0.7-1.0%. Since 1970, we examined chromosomal aberrations in 632 patients of the severely mentally and physically retarded. We recognized 21 cases of chromosomal aberrations (3.48%). Those are 11 cases of Down's syndrome, 2 cases of YY syndrome, one case of XXX female and one case of Turner's syndrome. And 6 cases are structural abnormalities. The frequency of chromosomal aberrations in this group is undoubtedly higher than in normal group. This fact is valuable for diagnosis and treatment of the severely mentally and physically retarded.

32. 重症心身障害児施設の小奇形スクリーニングによる染色体異常について： **池田琢哉・武居哲生・今村正人**（南九州病院・小児），**成富研二**（鹿児島大・小児）．
Chromosomal Aberration Found by Screening of Minor Anomaly in Homes for Severe Mentally and Physically Handicapped Children: Takuya IKEDA, Tetsuo TAKESUE, Masato IMAMURA (Minamikyushu Hosp., Kagoshima) and Kenji NARITOMI (Dept. Pediat., Univ., Kagoshima)

人間尊重と高度の社会福祉が求められつつある現在，重症心身障害児に対する医学的研究は，重要な課題であると考えられる．今回私たちは，167名の重症心身障害児を対象として，小奇形95項目を観察し，小奇形4個以上保有するものと，性器異常（停留睾丸，小陰茎，小さい睾丸，小陰唇の大きいものなど）のあるもの，および前記の該当者以外に大奇形が1個以上あり，小奇形を3個以上保有するものを対象の中からチェックした．上記のスクリーニング法でチェックされた44名について，染色体検査を実施した．その結果，小奇形観察の段階で診断のついたDown症候群3名と，5p－症候群1名，46,XX,16qh＋の異型染色体をもつ患児1名を発見した．なおDown症候群3名は，いずれも標準型の21トリソミーで，5p－症候群は父親の46,XY,t(4;5)(q35;p13)相互転座由来であった．なお16qh＋の症例は父親由来のもので，一般には16qh＋は二次狭窄部の過剰により，特徴的な臨床症状はないとされており，本症例は偶然発見された1例である．したがって，今回の小奇形スクリーニングによる常染色体異常頻度は，16qh＋を除くと，2.4%（4/167）であり，詳細な小奇形のチェックは，染色体異常を発見する一つの手段として重要であると思われた．

33. Cytogenetic Studies in Spontaneous Abortions: **Tsuyoshi HIASA, Ichiro KUSUMI, Katsunori UEDA, Koso OHAMA and Atsushi FUJIWARA** (Dept. Obst. Gynec., Hiroshima Univ., Hiroshima)

During a period from January, 1973 to June, 1978, 981 spontaneous abortuses were collected for chromosomal study in our Laboratory. Most of them were from the first trimester of pregnancy. In 766 specimens, materials were suitable for tissue culture. Of these, 505 were karyotypically examined and 237 specimens (46.9%) showed chromosome abnormalities. They were consisted of 130 of trisomy, 48 of triploidy, 40 of 45,X, 6 of tetraploidy, 5 of double trisomy, 4 of mosonomy 21, and 4 of miscellaneous abnormalities. Trypsin G-banding analyses of 119 trisomic specimens revealed different 20 types of autosomal trisomies, excluding trisomy 1 and 11. Among the autosomal trisomies, trisomy 16 was most frequently encountered (25.4%) and trisomy 22 and 21 were 8.5% and 7.7%, respectively. The relationship of phenotype of abortuses and chromosome abnormalities was also studied in the present series. Success ratio of karyotype analysis of empty chorionic sac and broken chorionic sac was 55.5% and its incidence of chromosome abnormalities was 29.7%. On the other hand, 74.1% of empty amniotic sac and intact sac with nodular embryo (1-4 mm) were successfully karyotyped and chromosome abnormality was found in 74.7% of karyotyped specimens. Conceptuses with autosomal trisomy compatible with live-birth, such as 13, 18, 21-trisomy showed a wide variation of develop-

ment, from an empty sac to an apparently normal fetus. In contrast to the above finding, conceptuses with other trisomy mostly showed an empty sac or a severely disorganized embryo, especially conceptuses with trisomy 16 were empty sacs without exception. It was also shown that triploid conceptuses tended to abort in rather late stage of the first trimester of pregnancy as compared with conceptuses with normal karyotype and other type of chromosome abnormalities. Sex ratio of specimens excluding 45,X and triploidy was 0.698 (169 males to 242 females).

34. 習慣性流産夫婦において認められた均衡転座染色体について： **末原則幸**（阪大・産婦），**林　弘子・大塚則光**（兵庫医大・中検），**橋本知子・古山順一**（兵庫医大・遺伝）． **Balanced Translocation in Couples with Repeated Spontaneous Abortions:** Noriyuki SUEHARA (Dept., Obst. Gynec., Osaka Univ., Osaka), Hiroko HAYASHI, Norimitsu OTSUKA (Dept. Cent. Clin. Lab., Hyogo Med. Coll., Hyogo), Tomoko HASHIMOTO and Jun-ichi FURUYAMA (Dept. Genet., Hyogo Med. Coll., Hyogo)

習慣性流産の既往を有する夫婦において，しばしば均衡転座染色体が見出されることはよく知られる．われわれは，2回以上の自然流産歴を有する婦人49人と夫45人について，染色体検査を行ったところ，13/14転座，14/15転座および7/12相互転座を有する症例を各1例経験した．均衡転座出現頻度は約6％である．D/D 転座の2例は，いずれも3回の自然流産を経験しており，生児を得ていない．過去の文献より，D/D 転座保因者の流産率は子供1人に対し，0.6～1.0 である．また D/D 転座保因者よりの D トリソミー出現頻度は，Hamerton によれば0.3％である．今回われわれが行った文献調査では，34家系119夫婦において4例の D トリソミーが認められた．転座保因者は175人，染色体正常者109人，染色体未検査97人であったが，発端者となった D トリソミー3例，転座保因者25例を除くと，D トリソミー出現頻度は0.4％，また正常と転座保因者の割合は4：5であった．7/12相互転座保因者の症例では，2回の自然流産のほか，正常女児1名，通常型ダウン症1名があり，さらに5回目の妊娠時の羊水診断によって7/12相互転座保因者と診断された．均衡型相互転座保因者の子における分離については不詳であるが，Boué らの38例の羊水診断で2例（5.5％）の染色体異常を診断している．このように，均衡型転座保因者から染色体異常児が生まれる危険率は，従来述べられていた値よりかなり低いと考えられる．

35. 抗てんかん剤 (Diphenylhydantoin) の細胞毒性： **鈴木康之・池田佳子**（国立武蔵療養所），**多田愛子・有馬正高**（同上・神経センター）． **Cytotoxity of Diphenylhydantoin:** Yasuyuki SUZUKI, Yoshiko IKEDA (National Musashi Sanatorium, Tokyo), Aiko TADA and Masataka ARIMA (National Center of Neuropsychiatric Disease, Tokyo)

主要な抗けいれん薬であるジフェニールヒダントイン (DPH) は，免疫能の低下や催奇形性など細胞機能を障害することが知られている．Herha and Obe は DPH 服用患者のリンパ球で，exchange タイプの染色体変異が亢進していることを報告している．われわれも同様に，DPH 服用群のリンパ球を48時間培養後に染色体標本とし，染色体変異率を検討した．さらに正常リンパ球を用いて，DPH

を 10μg/ml～30μg/ml となるように培養液に添加して，同様に48時間後に変異率の上昇をチェックした．DPH の血中濃度，培養液中の濃度は，酵素免疫法を用いて測定した．1）今回対象とした患者の DPH 血中濃度は全例 6μg/ml 以下であり，染色体の変異率はコントロール群よりも高かったが，統計的な差は認められなかった．2）染色体の変異率と服薬量・血中濃度との相関はともに認められないが，服薬量と相関する傾向が見られた．3）DPH 負荷による変異率の変化は有意であり，細胞毒性が肝臓での代謝産物や葉酸値の低下に基づくのではなく，直接作用していると思われる．4）Herha and Obe の報告と異なり，exchange タイプの亢進はとくに著明ではなかった．彼らの報告と異なった最大の問題点は，対象群の DPH 濃度が2倍以上違っていたためであると思われる．

36. Cytogenetic Studies of Granulopoietic Colonies in Chronic Myelocytic Leukemia: Yoshiaki SONODA, Tohru IDE, Kimikazu SAWAI, Hiromasa OGAWA, Shinichi MISAWA, Masuji MORITA and Tatsuo ABE (Dept. Med. and Dept. Prevent. Med., Kyoto Pref. Univ. Med., Kyoto)

This paper concerns with the cytogenetic studies on the granulopoietic colonies developing in methylcellulose culture of marrow and blood cells from 7 patients with CML. The Ph^1 chromosome was found in all patients. Granulopoietic colonies were obtained from marrow and blood cells by the method of Worton *et al.* with modifications. 2×10^5 nucleated cells were plated in 35-mm petri dish containing 1 ml of a mixture of alpha medium, 0.8% methylcellulose, 2% bovine serum albumine, 20% fetal calf serum, and 20% human placental conditioned media. Dishes were incubated at 37°C in a humidified atmosphere with 5% CO_2 in air. On the 7th day of culture, colcemid (0.2 μg/ml) was added. After 12 hr colonies and clusters were picked up using a fine Pasteur pipette. Cells were treated with hypotonic solution (0.075 mole KCL) for 60 min at 40°C, then fixed in methanol-acetic acid fixative for 15 min. After two changes of the fixative, resuspended cells were dropped onto clean and chilled slide glasses and dried by warm air. These preparations were stained with 2% Giemsa (pH 6.8) for 15 min. In the present study, granulopoietic colonies obtained from 7 patients with CML were analysed. Four of them were in remission, two were in the blastic crisis, and one was untreated. All metaphases from these 7 patients have the Ph^1 chromosomes and no Ph^1-negative cells were found. Analysable metaphases were too small to conclude whether the Ph^1-negative myeloid cell lines do exist in a dormant state in Ph^1-positive CML. The cytogenetic study on the granulopoietic colonies in CML will play an important role in this respect.

37. 化学物質で誘発した相互転座マウス個体の転座パターン：田中憲穂・大沢典子・室田哲郎・渋谷 徹・加藤基恵（食薬安全センター）．**Banding Patterns of Chemically-induced Reciprocal Translocations in Mice:** N. TANAKA, N. OSAWA, T. MUROTA, T. SHIBUYA and M. KATOH (Food and Drug Safety Center, Kanagawa)

BDF_1，9週齢の雄マウスに MMS (methyl methanesulfonate), 20 mg/kg, 50 mg/kg を腹腔内投

与し，1頭の雄に対し投与後1～20日の間に6頭の無処理雌と交配し F_1 を得た．得られた任意の F_1 につき妊性試験をしたところ，半不妊もしくは不妊マウスが 20 mg/kg 投与群で（90頭の F_1 のうち）3.3%，50 mg/kg 投与群で（152頭の F_1 のうち）12.5%生じた．組織学的には半不妊の一部および不妊マウスのほとんどが精子発生過程の途中で分化の停止が生じていた．これら妊娠低下のみられた F_1 雄マウスについて，第一成熟分裂の染色体分析を行ったところ，20 mg/kg 投与群で1頭，50 mg/kg 群で17頭に転座による多価染色体の対合がみられた．そして，この18頭の転座マウスのうち骨髄または精原細胞で明らかなマーカー染色体を有したのは3頭で，long chromosome 2例，Robertsonian 型転座1例であり，その他の転座マウスではマーカーを認めなかった．これら半不妊マウスのうち出産児が3～6頭で安定している6系統のラインを G-バンド法により転座染色体の同定を行ったところ，T1Ha の系が #2 と #17 の末端部の転座であることを確認したほか，T4Ha が #7 と #8，T5Ha が #13 の転座であることが示唆された．さらに，これら6系統の転座ヘテロマウスをそれぞれ正常雌と交配し，妊娠9.5～13.5日目に不均衡型染色体構成をもつと思われる胎児の死亡時期を調べ染色体の転座部位との関連を調べると，胎児の約半数が T1Ha で9日目，T2Ha, T3Ha, T4Ha, T5Ha で10日目，T6Ha で11日目に死亡していた．また出産児におけるヘテロ型と正常型の比はほぼ 1：1 であった．

38. G-Banding Analysis on Dose-Chromosome Aberration Relationship in A-Bomb Survivors (Preliminary Report): **Kazuo OHTAKI, Hachiro SHIMBA, Toshio SOFUNI and Akio A. AWA** (RERF, Hiroshima)

Using trypsin G-banding method, radiation-induced chromosome aberrations were analyzed in cultured lymphocytes derived from 9 A-bomb survivors of Hiroshima. A dose-aberration response relationship was established based on the frequency of detectable symmetric aberrations expressed as a function of dose, *i.e.*, $Y=a\cdot D^n$, where Y is the chromosome aberration frequency, D is the dose, n is the dose exponent, and a is a constant. Based on the observed aberration frequency, the following values were estimated for the model: $a=20.63\times10^{-4}$, $n=0.81$. The present findings were further compared with data from Hiroshima A-bomb survivors examined previously be the conventional staining method, yielding values of $a=10.55\times10^{-4}$, and $n=0.82$.

39. 新潟市西保健所における遺伝相談について： **富樫和夫・青木英子・北村ハル・浅間淳子**（新潟市西保健所），**本多達雄**（新潟大）． **The Role of Paramedical Stuff in Genetic Counseling in Niigata City:** K. TOGASHI, E. AOKI, H. KITAMURA, J. ASAMA (Nishi Health Center of Niigata City, Niigata) and T. HONDA (Niigata Univ., Niigata)

新潟市西保健所では，昭和46年から「結婚医学相談室」を開設していたが，その中には遺伝に関する相談も少なくなかった．そこで昭和48年の新潟大学産婦人科における遺伝外来開設を機に下準備をはじめ，昭和51年2月に当市保健所助産婦保健婦に対するパラメジカルスタッフとしての研修会を行った．当所での遺伝相談業務は昭和51年6月に開設し，現在月2回，1日3人の時間予約制をとっている．広報紙「市報にいがた」で一般に公示し，相談希望者は電話で予約する際に相談内容の概略を

話し，助産婦は疾病状況等によって振り分ける．なおナンセンスコールについては一応の指導をし，予約はしない．現在まで2年間に実人員75人，延人員は92人の相談ケースがあった．相談の疾患は多岐にわたっているが，精神神経系疾患が1/3を占め，また自分の子供が発病者である場合の相談が最も多くなっている．相談来所者の心理についてのアンケートでは，その2/3が今までにきちんとした指導を受けたことがなく，また市報や新聞を見て直ちに申し込んだ者70%，予約時から相談までの気持ちは，申し込んだだけで安心したとか，相談日が待ち遠しかった者65%，相談後は来てよかった，一応の目途がついた者，合わせて94%となっている．以上のように，地方都市の保健所でもパラメジカルスタッフの配置により遺伝相談が可能と考えられる．ただし，カウンセラーの関係から大学等の協力は必要である．

40. 産婦人科における遺伝相談（妊婦の遺伝相談）：高内則男（済生会新潟），**本多達雄・竹内正七**（新潟大・産婦）．**Analyses of Genetic Counseling in Our Department of Obstetrics and Gynecology:** Norio TAKAUCHI (Saiseikai Hosp., Niigata), Tatsuo HONDA and Shoshichi TAKEUCHI (Dept. Obst. Gynec., Niigata Univ., Niigata)

近年遺伝相談の必要性が各方面から要望され，遺伝相談システムも関係者の地道な努力により着々と確立され成果を上げつつある．新潟大学産婦人科外来においては，昭和48年2月より遺伝外来を開設し現在まで微力ながら相談業務を続けており，カルテ作製に至った件数は364件となっている．このうち妊婦の占める割合は129人，約35%であった．そこで今回は妊婦における遺伝相談に関して，その特徴や内容について報告をする．1）遺伝相談件数の推移をみてみると，昭和48年は41件で，以後漸次増加し昭和52年は99件，昭和53年6月現在55件となっている．2）遺伝相談時年齢分布は26～30歳が最も多く次いで21～25歳となっており，全国の年齢別出生率とほぼ一致し年代によるかたよりはなかった．3）遺伝相談時妊婦の初産経産別区分では，初産59例，経産90例であった．4）妊婦における遺伝相談を内容別にみると，薬物と妊娠が41例，前回異常児分娩27例，妊娠とX線17例，妊娠と感染症14例，本人または配偶者の異常9例，家族の異常8例，高年齢妊娠7例，近親婚2例等であった．妊婦における遺伝相談では薬物の影響，X線，感染症などについての相談が多く，妊娠するまではあまり気にならなかったようなことが，妊娠したという事実を境にして非常に心配になり相談に訪れる傾向が強いようであった．

41. 長崎地区の遺伝相談：馬場輝実子（国療・長崎病院・児），**貞森直樹**（長崎大・原研内），**錬石昇太郎**（放影研・内）．**Genetic Counseling in Nagasaki:** Kimiko BABA (Dept. Ped., Nat. Sanatorium Nagasaki Hosp., Nagasaki), Naoki SADAMORI (Dept. Med., Atom. Bomb Dis. Inst., Nagasaki Univ., Nagasaki) and Shotaro NERIISHI (Rad. Effects Res. Found., Hiroshima)

長崎地区の遺伝相談が昭和48年4月長崎市医師会館に設置されて以来，本年3月で5年になった．毎月1回，第3土曜日に予約による平均3件の相談を受け，5名の医師（内科・小児科・精神科・皮膚科）が交互に担当し，すべて無料で行っている．この5年間に50回，146件の相談があり検討してみた．相談内容は小児科27.7%，内科13.5%，眼科12.3%，精神科9.7%，整形外科8.4%，耳鼻科7.7%，皮膚科6.5%，その他5.7%．結婚に関しては49件で33.6%，内容的には血族結婚というよりはむしろ遺伝性疾患に対する不安が強く現れていた．来談者は213名で男93名，女120名．年齢的には

20代の女が最多で，結婚適齢期および異常児をもつ母親にみられた．地域別では長崎市内が62%を占めたが，およそ長崎県全体におよび，県外は4.8% であった．われわれの遺伝相談は新聞，ラジオなどのサービス情報を得て来談するのがほとんどで紹介は18%にすぎない．来談後の follow up ができていないが，一応結論としての答えが出されたもの73.3%，そのうち再来によるもの8.2%，問題が残されたまま結論が出ていないもの11.6%，ナンセンス・コール15.1%であった．長崎は他の地域とことなり被爆地であり，被爆2世の問題は深刻である．長崎の場合は医師会で行っているという特質を生かして，地域の遺伝相談室としてさらに発展させようと思っている．

42. 遺伝相談センターにおける1年間の相談例： **大倉興司**（東医歯大・難研・人類遺伝），**半田順俊**（和歌山医大・解剖）． **Counseling for a Year in the Genetic Counseling Center in Tokyo:** Koji OHKURA (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo) and Yoshitoshi HANDA (Dept. Anat., Wakayama Med. Coll., Wakayama)

厚生省の家族計画特別相談事業によって1977年10月日本家族計画協会に設置された遺伝相談センターで本年9月末までに扱った1年間の相談状況を要約する．相談の問合わせは全国にわたり計2,059件で，そのうち527件の面接を行い，一部は他の機関へ紹介した．面接の527件について，クライアントは男131，女344，年齢の分布は20歳代が49%，50歳以上が16%で2峰性となる．相談の方法は原則として面接で445，視力障害その他で手紙，電話によるもの82件である．センターの所在の情報源はマスコミによるものが半数を占め，一方医療関係より紹介されたものは16%にすぎない．地域別では東京が半数で，これに神奈川，埼玉，千葉，静岡を合わせて全例の79%を占める．申し込みから面接までの所要時間は平均13.8日，約2週間である．面接回数はおおむね1回ですますようあらかじめ情報の収集に努力しているが，2回16件，4回が1件ある．面接時間は最短15分，最長150分，平均55分である．相談の時期は結婚前 247 (55%)，妊娠前 131 (31%)，妊娠中 (0.9%)，その他23となる．クライアントと患者の関係は近親婚を除いた461例で，本人の血族に患者のあるもの 27%，子供が患者のもの26%，本人が患者のもの17%，計60%で，残り40%が配偶者およびその関係者である．疾患の種類は445例中，先天奇形(兎唇口蓋裂を含む) 29%，精神性疾患14%，これにてんかん，精神薄弱を加えると23%，色覚異常8%，染色体異常5%，聴覚障害，代謝異常，眼疾患，皮膚疾患それぞれ4%，ほかに神経筋疾患，症候群，血液疾患，放射線の影響等である．近親婚は527例中88件で，そのうち 67 (76%) が近親婚の一般問題に関するもので，家族中に異常を認めるものが 21 (24%) に当たり，異常の種類はまちまちである．

43. Genetic Counseling. VII. Followup Study: **Norio FUJIKI, Hidetsune OISHI, Itsuro NISHIGAKI, Reiko TSUKAHARA, Yasuko SHIRAI** (Dept. Genet., Epidemiol. & Soc. Welf., Inst. Develop. Res., Kasugai), **Hideko MASUDA** (Asuke Health Cent., Asuke) **and Isamu KIMURA** (Shukutoku Coll., Nagoya)

We have reported on the recent trends of the genetic counselling in our institutions and briefly on the followup study of this service at the last meeting. This time, we have analyzed these data in detail. Among 125 consultations carried out in the years 1969-75, followup study was successful in 81 families (64.8%), as reported last year. In order to

clarify the bias of the response for this questionnaire, we have checked all data of our 388 counselling cases by the year of counselling, sex, age, motive of the client, content and risk estimation, and it was concluded as follows: 1) The questionnaires should be reached in 2 or 3 years after consultation, in order to clarify the reproductive performance followed by our advice. 2) The parents with defective childbirth, and the clients who asked about inherited disease or visited at the time of their pregnancy, have responded very cooperatively. 3) No bias was revealed in the response between groups with high and low risk in each category. Our followup data represented that a large majority of the clients had accepted the advice in their reproduction at the satisfactory level.

44. 遺伝相談の効果判定に関する研究：竺原俊行（大阪市立母子センター），**大倉興司**（東医歯大・難研・人類遺伝）. **Evaluation of Genetic Counselling:** Toshiyuki JIKUHARA (Osaka City Maternity Center) and Koji OHKURA (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo)

遺伝相談の効果判定は，カウンセラーの行った遺伝相談をクライアントが正しく理解し，自らの意志決定を見とどけるところにあると思われる．今回遺伝相談の質的向上をはかることを目的として，アンケート形式により，現在われわれの行っている遺伝相談に対するクライアント側の評価を多面的に求めてみた．すなわち，昭和53年3月より8月までに，日本家族計画協会遺伝相談センター，大阪市立母子センターを訪れた人を対象とし，遺伝相談終了後1カ月以内に，その時点での考えを記入して発送するよう依頼した．まず遺伝相談施設の存在は，過半数が新聞，ラジオという報道機関を通じて知り，遺伝相談を受けるまでの期間については長い間心配してきた者が過半数を占め，受け入れ側の遺伝相談の申し込みは大部分の人が気軽に受け付けてもらった，十分に話ができた，理解できた，と返答をよせている．さらに危険率に対するクライアントの評価では10%以上では，その危険率を低いと評価する者はなかった．遺伝相談を受けた後の意志決定については約半数が決定しており，考慮中，もう一度相談してからといった未決定が約30%あり，本調査が遺伝相談後1カ月以内では少し早いのかもしれない．遺伝相談を受けた結果については大部分の人が，よかった，適当な相談時間，と返答していた．以上，アンケートより見る限り，われわれの行っている遺伝相談に対するクライアントの反応がほぼ満足すべきものであることを確認した．さらに今後の追跡調査に対して過半数が協力を申し出ている．このような人々に応えるためにも，よりよい遺伝相談をめざして検討していきたいと考えている．

45. Inevitable Uncertain Informations in Genetic Counseling: Koji OHKURA (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo)

In genetic counseling, correct medical, biological and genetic informations are highly requested. However, it is impossible to exclude uncertain informations in the counseling. For example, a genetic counselor and his supporting medical associates are often unable to examine the affected individual(s) as key person(s) in the counseling. In a year from 1977 to 1978, the Genetic Counseling Center of Japan Family Planning Association in Tokyo received more than 2,000 cells and 527 counselings have been done. Excluding

the cases concerned with consanguinity, 80 of 461 counselees (17%) were affected. In 571 counselees and his or her families, only 77 individuals (13%) were examined by the genetic counselor(s). Only 28 cases (5%) brought the medical certificate or the medical records. Other counseling cases (82%) were based on hearsay evidences. Also blood relationship or pedigree was almost always based on hearsay evidences. When misdiagnosis by a genetic counselor and his medical team could be minimized, identification of diagnosis by other physicians is very difficult. The author indicates several potential sources which will lead miscounseling.

46. 遺伝相談における先天奇形診断のすすめ方：木田盈四郎（帝京大・小児）. **Diagnostic Technique of Congenital Malformation Syndrome:** Mitsushiro KIDA (Dept. Pediat., Teikyo Univ., Tokyo)

先天奇形についての遺伝相談に応ずるまえに，患者の正しい診断が必要である．正確な診断が必要な理由は，1) 正しい治療に役立つ，2) 診断がつかぬために行われる余計な検査や治療が避けられる，3) 患者の予後が分かり，手術，リハビリテーション，学校教育などに役立つ，4) 患者の隠された障害が予測され，その早期対策に役立つ，5) 患者の同胞や子供に現れる再発危険率が予測され遺伝相談に役立つ，などである．診断の順序は，病歴，理学的検査，補助的検査，経過の観察などからなる事実の収集と，その分析として，収集した資料の評価，所見の重要度に応じた配列，中心となる特徴の選択，この特徴に一致する疾患の列記，これらの疾患の中から最終的診断名の選択，すべての根拠の再検討などからなる．診断名がついてから，その疾患が遺伝病として報告されているか，さらにどのような遺伝様式をとるか調べるが，それには，常染色体優性遺伝病 583，常染色体劣性遺伝病 446，X 連関遺伝病93が収録されている，McKusick; Mendelian Inheritance in Man. The Johns Hopkins Univ. Press, 1975 が便利である，臨床家は，患者を診察したならば少なくとも，最終的にその患者が遺伝病，染色体構造異常，染色体数異常，胎芽病，胎児病，周生期障害の 6 つの分類のすべてについて，A：確かである，B：可能性がある，C：違うと思われる，D：違う，E：分からない，の一つの選択を求められている．

47. Evaluation of Mutagen-Metabolizing Capacity of Cultured Mammalian Cells, as Revealed by the Induction of Chromosome Aberrations and Sister Chromatid Exchanges: Tatsuro IKEUCHI, Keiko SUGIMURA and Motomichi SASAKI (Chrom. Res. Unit., Fac. Sci., Hokkaido Univ., Sapporo)

It is well known that many environmental mutagens are biologically inert themselves, but require some form of metabolic activation before they become effective. For screening such indirect mutagens several experimental systems have been employed, such as a host-mediated assay and a liver microsome activation system *in vitro*. In order to develop more simplified *in vitro* test systems, we have attempted to search for cultured mammalian cells which are capable of metabolizing indirect mutagens, without introducing the exogenous activation systems. As indicators of the metabolic capacity, chromosome breakages

(CB) and sister chromatid exchanges (SCE) were used. Three indirect mutagens were used: cyclophosphamide (CP, at concentrations of 5×10^{-5}-5×10^{-3}M), dimethylnitrosamine (DMN, 10^{-4}-10^{-1}M), and benzo(a)pyrene (BP, 10^{-6}-3×10^{-4}M). At present, the following 10 cell lines have been tested: 4 lines of rat ascites hepatoma cells (AH66-B, AH 66-C, AH70B, AH109A), Yoshida sarcoma cells in culture, a line of Chinese hamster embryonic fibroblasts (B-13), 2 lines of human embryonic fibroblasts (HE2144, HE2236), a cell line derived from a human esophageal cancer (TH), and a Burkitt lymphoma cell line (P3HR-1). Out of the 10 cell types tested for the response to CP, 4 lines of rat ascites hepatoma and Yoshida sarcoma cells showed a significant increase in frequencies of both SCE and CB with a clear dose-relationship: At the highest concentration (3 or 5×10^{-3}M), the yield of CB in these cell types were 20 to 40 times higher than the control levels, and the highest SCE frequency obtained for AH70B was as high as 9 times the control value. Human and Chinese hamster embryonic fibroblasts were moderately sensitive to CP, but the response in TH and P3HR-1 was almost negative or extremely low. Among the cell types tested with DMN or BP, the AH66-B rat hepatoma cells were effective to both the mutagens in the induction of CB, though no significant SCE induction was observed. P3HR-1 and HE2144 were ineffective to either DMN or BP in the induction of both CB and SCE, while B-13 cells showed a slight increase in the SCE frequency after BP treatment. The above findings suggest that certain types of cultured mammalian cells, especially the rat hepatoma cell lines, are efficient in converting indirect mutagens into the active form, in terms of the induction of SCE and chromosome aberrations. This study was supported by a Grant-in-Aid for Cancer Research from the Ministry of Education, Science and Culture of Japan.

48. Studies on the Detection of Unknown Mutagens by the Induction of SCEs in Human Lymphocytes and Evaluation of Their Relative Risk by the Method: Tatsuo ABE, Masuji MORITA, Hiromasa OGAWA, Shinichi MISAWA, Kimikazu SAWAI, Tohru IDE and Yoshiaki SONADA (Dept. Prevent. Med. and Dept. Med., Kyoto Pref. Univ. Med., Kyoto)

The detection of sister chromatid exchanges (SCEs) has been suggested to be useful in the detection of unknown mutagens and carcinogens. By using FPG technique we have reported the frequencies of SCEs induced by Busulfan *in vivo* and *in vitro* and also by some metal compounds such as $CrCl_3$, $K_2Cr_2O_7$, K_2SeO_3, K_2SeO_4, Na_2AsO_2 and $NaHAsO_4$. This paper is concerned with some other metal compounds such as $HgCl_2$, CH_3HgCl, $CdCl_2$, $NiSO_4$, $MnCl_2$ and K_2MoO_4 and some anti-tumor drugs which include MMC, Bleomycin, Dibromomannitol, Pipobroman and FT-207. Two known carcinogens of 4NQO and MNNG were also examined as a positive control. All experiments were performed on the blood cells taken from a normal individual. The frequencies of SCEs in normal

subjects ranged between 6.25 and 7.76 per metaphase cell with a mean value of 6.92±1.19. The yields of SCEs induced by 4NQO, MNNG, MMC, Busulfan and DBM *in vitro* showed a dose-related increase. Among them the highest increase of SCEs were observed in DBM in a molar concentration of 10^{-6} with a number of 47.48 per cell. The highest number of SCEs induced by the other chemicals were as follows: MMC in 10^{-7}M, 30.40; 4NQO in 10^{-5}M, 24.48; and MNNG in 10^{-4}M, 20.20. We have also examined the frequencies of SCEs in blood cells from the patients with cancer or leukemia who had been treated with the chemotherapeutics (*in vivo* study). DBM was also found to induce the highest SCEs, being followed by BENP (Bleomycin, Cyclophosphamide, Procarbazin, and Predonisone), MMC, Bleomycin, Cyclophosphamide, Pipobroman, Busulfan, DCMP (Daunomycin, Ara-C, 6-MP, and Predonine), FT-207 in the order of frequency. On the other hand, SCEs induced by metal compounds showed no remarkable increase, and sometimes had no dose-dependency. On the basis of these observations, the SCE-test as a possible test system for the detection of unknown muta-carcinogens was discussed.

49. Effects of Chemicals on SCE Rate and Cell Cycle Kinetics in Human Lymphocytes: Toshiaki WATANABE and Akira ENDO (Dept. Hyg. Pred. Med., Yamagata Univ., Yamagata)

In this study, the cytogenetic effects of some environmental heavy metals on SCEs were examined with special reference to their effects on cell-cycle kinetics. Human lymphocytes were grown in PHA-stimulated TC 199 medium supplemented with 20% of fetal calf serum for 72 hr at 37°C in the dark. Bromodeoxyuridine was added at the beginning of the culture at a final concentration of 10 μg/ml. Chemicals were added in two different concentrations; methylmercuric chloride (CH_3HgCl) and mercuric chloride ($HgCl_2$); 10^{-4}M and 10^{-5}M, cadmium chloride ($CdCl_2$); 10^{-5}M and 10^{-6}M, cadmium sulfide (CdS); 10^{-6}M and 10^{-7}M. Also, for a positive control, mitomycin C (MMC) was added at concentrations of 10^{-7}M and 10^{-8}M. The lower levels of concentrations were selected so that the proportion of the second division metaphases should be in the same range of 0.4-0.5 for each chemical, and the higher dose levels were ten times the lower levels. Chromosome preparations were made by the conventional air-drying method and differential staining of sister chromatids was carried out by the modified FPG method. Although no effect on the SCE rate was observed in $HgCl_2$-treated lymphocytes or cadmium compounds-treated lymphocytes, the SCE rate increased in CH_3HgCl-treated lymphocytes (13.4±4.0 s.d. for 10^{-4}M and 11.6±3.3 for 10^{-5}M) as compared with that of the untreated control (9.7 ±2.7). However, when this SCE rate was compared with that of the positive control of MMC-treated lymphocytes (30.8±11.7 for 10^{-7}M and 14.2±4.2 for 10^{-8}M), the observed increase should be regarded as relatively slight. The present findings indicate that the

analysis of the cell-cycle kinetics may be informative as one of indicators of cytotoxic effects for setting of dose levels for the analysis of SCE induction by environmental chemicals.

50. Bloom 症候群細胞の姉妹染色分体交換ならびに染色分体交換に及ぼすマイトマイシン C の影響：白石行正 (高知医大・解剖). **Effect of Mitomycin C on the Sister Chromatid Exchanges and Chromatid Exchanges in Bloom's Syndrome Cells:** Yukimasa SHIRAISHI (Dept. Anat., Kochi Med. Sch., Kochi)

高発癌性劣性遺伝病 Bloom 症候群では，培養末梢血細胞において hemologous chromatid interchange (HCI) が確認できるが，演者のこれまでの研究では，骨髄，皮膚細胞には必ずしも HCI は見られていない．一方，BUdR を用いた姉妹染色分体交換 (SEC) の頻度はいずれの組織においても細胞あたり 70～80 SCE と，異常に高く，平均でも正常のそれと10倍もの差が見られた．これらの所見をもとに演者らは，Bloom 症候群の最も重要な特徴は高頻度 SCE であると結論した．マイトマイシン C は，正常細胞において HCI と SCE 両方を引き起こすことで知られている．マイトマイシン C による HCI は No. 1, 9, 16 染色体の動原体部位で quadriradial を形成しており，この意味では Bloom 末血細胞に spontaneous に見られる HCI とは異なっていると思われる．そこで，Bloom 細胞にマイトマシン C 処理することにより，どのように HCI, SCE が変化するかを調べた．0.05, 0.1μg/ml MMC 処理では，正常細胞では HCI の増加が顕著ではなかったが，Bloom 細胞では有意に高頻度の HCI が見られた．正常細胞では No. 1, 9, 16 染色体に HCI が見られたが，Bloom 細胞ではこれらの染色体のほか No. 2, 3, B, D, 17, F, G 染色体に HCI が見られた．以上の観点から，正常および Bloom 細胞に対するマイトマイシン C の感受性を SCE ならびに HCI の立場から追求した．

51. ダウン症候群患児の培養リンパ球に対する塩化カドミウムの影響：保科弘毅 (杏林大・小児)，**田村高志** (杏林短大・細胞遺伝)，**日暮 真** (東大・産婦). **Effects of Cadmium Chloride on the Cultured Lymphocytes from Patients with Down's Syndrome:** Hiroki HOSHINA (Dept. Pediat., Kyorin Univ., Tokyo), Takashi TAMURA (Div. Cytogenet., Kyorin Med. Technol. Coll., Tokyo) and Makoto HIGURASHI (Dept. Matern. Child Health, Univ. Tokyo, Tokyo)

重金属のダウン症候群患児染色体に及ぼす影響を知る目的でダウン症候群患児より得た末梢リンパ球に塩化カドミウムを添加して培養し，Korenberg と Freedlender の方法を用いて，その姉妹染色分体交換 (SCE) の頻度を検討した．年齢1～3歳の正常対照群5例と21トリソミー型のダウン症候群5例を選び，末梢血をヘパリン採血し，全血のまま 0.1 ml ずつ5本の試験管に分け，20% FCS, PHA, 1×10^{-4} モルの BudR を含んだ T.C. 199 培養液を加え，さらに塩化カドミウムを最終濃度が 1×10^{-4} モル，1×10^{-5} モル，1×10^{-6} モル，1×10^{-7} モルとなるよう添加し，1本を無添加対照として72時間暗所で培養し，染色体標本を作製した．この標本を2日間暗室に放置した後，姉妹染色分体の染め分けを行った．各濃度について1症例，少なくとも5細胞以上平均10細胞合計50細胞について検討を行った．正常対照群では塩化カドミウム無添加対照の SCE の頻度4.36±1.48と比較し，1×10^{-4} モルでは 4.20±0.66，1×10^{-5} モルでは 4.20±1.05，1×10^{-6} モルでは 4.06±0.76，1×10^{-7} モルでは 3.92±0.72 といずれにおいても SCE 頻度の増加は認められなかった．ダウン症候

群症例においても塩化カドミウム無添加対照における SCE の頻度 4.20±0.80 と比較し，1×10^{-4} モルでは 4.04±0.72，1×10^{-5} モルでは 4.00±0.69，1×10^{-6} モルでは 3.94±0.73，1×10^{-7} モルでは 3.96±0.66 といずれの濃度においても SCE の頻度の増加は認められなかった．塩化カドミウムを同じ濃度で添加培養して染色体切断をみてみると，正常対照群では明らかな差はないが，ダウン症候群症例では 1×10^{-4} モルの濃度で明らかに染色体切断頻度の上昇が認められた．以上の結果は，ダウン症候群においては染色体切断誘発のメカニズムと SCE の形成との間には直接的な関連がないことを示唆している．

52. ヒトの培養リンパ球における放射線による染色体不分離：大屋幸子（神奈川衛生短大），**佐々木正夫**（京大・放生研），**外村　晶**（東医歯大・難研）．**Induction of Chromosomal Nondisjunction by Radiation in Cultured Human Lymphocytes:** Y. OYA (Kanagawa Pref. Coll. Hygiene, Yokohama), M.S. SASAKI (Rad. Biol. Center, Kyoto Univ., Kyoto) and A. TONOMURA (Dept. Cytogenet., Tokyo Med. Dent. Univ., Tokyo)

染色体の異数性を主体とするゲノム突然変異は，染色体異常による先天異常疾患の中でも主要な位置を占めており，その成因に対する物理的，化学的な外的要因の係わり合いとその障害度の量的評価は従来より繰り返し問題となっているところである．今回私どもは，^{60}Co γ-線をヒトの培養リンパ球に照射し，照射後の細胞分裂に伴う染色体不分離を調べた．培養開始20時間後のリンパ球に 0，100，200，300 R の γ-線を照射し，BUdR (40 μM) 存在下でさらに52時間培養し，標本を作製した．Hoechst-Giemsa 法で姉妹染色分体を分染し，分染様式から識別できる第1回，第2回，第3回目の分裂中期における染色体数および構造異常を観察した．その結果，第1回目と第2回目の高2倍性細胞の頻度の増加分から，照射後第1回目の分裂時に誘発された不分離頻度が求められ，その値は1分裂当り，0R の場合 0，100R の場合 0.014，200R の場合 0.010，300R の場合 0.047 となり，高線量になるにつれて増加する傾向がみられた．しかし線量との詳細な関係は不明である．また第3回目の分裂中期の細胞から，第2回目の分裂時にも比較的高頻度の不分離が誘発されるという予想外の結果が得られた．これらの点に関して今後さらに明らかにしていく予定である．なお，不分離の誘発が予想される化学物質 (diethylstilbestrol; 50 μg/ml，コルセミド; 0.014 mg/ml，塩化メチル水銀; 2 μg/ml) を用いて同様の実験を試みた結果，いずれも1分裂当り 0.02～0.05 の不分離誘発が観察された．

53. Aneuploidy and Ageing—Premature Centromere Division of the X Chromosome: Akira TONOMURA, Kunikazu KISHI, Hisako OCHI and Fumiko SAITO (Dept. Cytogenet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

It is generally accepted that the frequency of aneuploid cells in cultured blood lymphocytes increases with age and this feature is more marked in females than in males. The substantial increase in aneuploidy with age in females is associated with non-disjunction of the X chromosome and it is considered that the premature centromere division of the X chromosome (PCD'X') may be a mechanism of mitotic non-disjunction. In the present study, we have examined the frequency of cells with PCD'X' in cultured lymphocytes

obtained from healthy women aged from 30 to 80 years. The peripheral blood lymphocytes were cultured with NCTC 109 and PHA for 48 hr. Chromosome analyses were carried out by the use of photographic method. The frequency of 46-cells with PCD'X' increased significantly with age (0.4% for 30 yrs group and 3.1% for 80 yrs group). Most a single chromosome was involved, but in some cells both X chromosomes had PCD. The 47-cells with a PCD'X' increased in 50 yrs group and then decreased in older groups. The frequency of 47-cells with two PCD'X' showed no increase with age. On the other hand, the proportions of cells with 47,XX,+C showed an increase with age, with a maximum of about 0.8% in 70 and 80 yrs group respectively. The C group chromosome was not identified but most of them was considered to be the X chromosome. Therefore, it seems likely that the PCD may be a part of mechanism of mitotic non-disjunction contributing to the increase in 47,XXX cells with age.

54. 母体の加齢にともなう染色体不分離の増加とその解析： 舟木賢治・菅原茂樹・美甘和哉（旭川医大・生物）． **An Analytical Study on the Chromosomal Nondisjunction Increasing with Advanced Maternal Age:** Kenji FUNAKI, Shigeki SUGAWARA and Kazuya MIKAMO (Dept. Biol. Sci., Asahikawa Med. Coll., Asahikawa)

母体の高齢化にともなって増加する染色体不分離に関し，以下の点はまだ明らかでない．1）染色体異常が生ずる卵子形成期，初期卵割期，それぞれにおける不分離頻度．2）それぞれの染色体についての不分離頻度．そこで，染色体が明瞭な形態的特徴から3群に分類されるチャイニーズハムスターを用い，妊性を確認した生殖適齢期の母獣（6～8月齢，対照群）および6～8産を経験した生殖衰退期の母獣（16～19月齢，老齢群）の2群から採取した第2卵母細胞と2細胞期胚について染色体分析を行った．第2卵母細胞における異数体出現頻度（第1成熟分裂の染色体不分離頻度）は，対照群 1.4%，老齢群 4.1% で，その差は有意であった（$p<0.02$）．2細胞期胚における異数体出現頻度（第1・第2成熟分裂および精子由来の不分離頻度）は，対照群 2.1%，老齢群 5.2% で有意差を認めた（$p<0.05$）．またモザイク出現頻度（第1卵割での不分離頻度）についても，老齢群 3.9%，対照群 0.9% で前者が有意に高かった（$p<0.02$）．以上の結果から，次のことが明らかとなった．1）母体の高齢化は，第1成熟分裂と第1卵割で染色体不分離を顕著に増加させるが，第2成熟分裂における増加は顕著ではない．2）染色体不分離は，第1成熟分裂で最も多く，続いて第1卵割，第2成熟分裂の順であった．また，不分離を起こした染色体を同定した結果，染色体不分離は上述した染色体のすべての群で起こり，特定の群に多発する傾向はないことが明らかとなった．さらに，高数性と低数性はほぼ同じくらいの頻度で生ずることも，この研究で認められた．

55. 母体の高齢化にともなう一価染色体増加と染色体不分離との関連に対する反証：菅原茂樹・舟木賢治・美甘和哉（旭川医大・生物）. **Disproof of the Relationship between Chromosomal Nondisjunction and Univalents in Oocytes of Aged Animals:** Shigeki SUGAWARA, Kenji FUNAKI and Kazuya MIKAMO (Dept. Biol. Sci., Asahikawa Med. Coll., Asahikawa)

母体の高齢化と異数体出現率の増加との関連について Henderson and Edwards (1968) は，マウスの老齢母獣の卵子の第1成熟分裂中期では相同染色体が互いに分離して一価となるものが増加し，この一価染色体の異常行動が第1成熟分裂における染色体不分離の原因であると提唱した．他の研究者により一価染色体の出現頻度の増加は再確認されたが，最近の報告では不分離との関連については異論があり，結論が得られていない．そこで，われわれはチャイニーズハムスターを用いて，第1成熟分裂中期における一価染色体を同定し，第2成熟分裂中期における異数体の異常染色体との間の関連を検討した．染色体をその大きさと形態的特徴から，大形中部着糸型：A群，端部着糸型：B群，小形中部着糸型：C群の3つのグループに分け，一価染色体と不分離染色体の出現頻度を3群の間で比較した結果，一価染色体はA群の1例（0.09%）をのぞき他はすべてC群（3.0%）で出現していた．それに対して，染色体不分離はA群（0.23%），B群（0.6%），C群（0.38%）のいずれの群でも生じていて，B群でやや高い頻度を示しているがグループ間に有意差はなかった．このことは，一価染色体を形成する染色体でとくに不分離が起こる傾向がないことを示している．以上の結果は，一価染色体形成と染色体不分離との間には直接的関係がないことを示しており，Henderson らの仮説を肯定することができなかった．

56. 過排卵誘発と染色体異常：小出展久・上口勇次郎・美甘和哉（旭川医大・生物）. **Chromosomal Aberrations after Superovulation:** Nobuhisa KOIDE, Yujiroh KAMIGUCHI and Kazuya MIKAMO (Dept. Biol. Sci., Asahikawa Med. Coll., Asahikawa)

過排卵誘発処理後に得たチャイニーズハムスターの卵の第二成熟分裂中期染色体を分析し，この処理が第一成熟分裂における染色体の行動に影響するか否かの検討を行った．発情期の午後2時にPMS 0.1 IU/gBW を腹腔内注射し，48時間後，HCG 0.2 IU/gBW を同様に投与した．さらに20時間後，排卵された卵管卵を輸卵管膨大部より，排卵に至らなかった卵巣卵を成熟未排卵濾胞より，それぞれ採取した．過排卵誘発処理を受けた個体のうち，11個以上排卵した31頭について染色体分析を行った．採卵された620卵のうち，分析可能な卵は580卵（93.5%）であり，異数性，倍数性，染色体切断などの染色体異常は計4.1%であった．これは対照群の2.6%（447卵中11卵）に比べると，増加傾向を示しているが有意差は認められていない．しかし，その不分離の頻度を総染色体数に対する不分離回数として表してみると，ここでは有意差（$p<0.01$）が認められたので，さらに例数を増せば卵単位の染色体異常出現についても有意差がみられることが示唆される．成熟未排卵濾胞より採取した卵巣卵ではこれらの傾向がさらに著しくなり，すべての異常卵（6.4%）についてみても，また異数性（5.9%）だけについてみても有意差が認められた．過排卵処理で成熟させた濾胞のなかには，染色体異常が多く含まれることが示されたが，その多くは排卵されないまま卵巣内に残されていた．しかし，この現象は今回のホルモン処理にみられた結果であり，処理如何によってはこれらの卵巣卵が排卵される可能性も否定できない．また排卵された卵管卵については，充分な結論と言えないまでも，ある程度染色体異常の増加することが示唆された．

57. Quantitative Analysis of Chromosome Variants in Man. I.: Jun-ichi AZUMI, Yasuo NAKAGOME and Ei MATSUNAGA (Nat. Inst. Genet., Mishima)

In the Paris Conference, the use of a numerical designation, 1 to 5, was recommended for the purpose of recording the size of a variant. However, no specific definitions were given for the individual digits. As to the qh regions of nos. 1, 9 and 16, the use of size relative to either a 21q (Müller *et al.*) or a 16p (Patil and Lubs) was proposed. The ratios thus obtained were assigned more or less arbitrarily into five digits. In the present study, size of qh regions was measured using a microdensitometer. A variety of criteria, including those of Müller *et al.* and Patil and Lubs, were compared. Both criteria gave consistently higher scores for 1qh regions, most of them being 3 or 4, than those for both 9qh or 16qh regions. On the other hand, most 16qh scored either 2 or 1. It is reasonable to expect that a score for a particular qh region with an average size is 3 in the Paris Conference (1-5) system. In addition, the score of each variant should be based on how different they are from an average, *i.e.*, they should be defined in terms of the standard deviation (SD). A system is described in which "score 3" corresponds to within ± 1 SD of an average of each 1qh, 9qh or 16qh region. Scores 2 and 4 are within ± 2 SD (except for those within ± 1 SD), Scores 1 and 5 outside ± 2 SD. It appears that more variants can be detected by the present system than any other methods tested.

58. 画像解析機による Ph^1 染色体の測定：田中公夫・大北　威（広島大・原医研・血液），**鎌田七男・蔵本　淳**（広島大・原医研・内科）. **Measurement of Ph^1 Chromosome by Means of Image Analyser:** Kimio TANAKA, Takeshi OHKITA (Dept. Haemat., RINMB, Hiroshima Univ., Hiroshima), Nanao KAMADA and Atsushi KURAMOTO (Dept. Int. Med., RINMB, Hiroshima Univ., Hiroshima)

分染法の開発により，個々の染色体の識別は容易かつ確実なものになり染色体の質的変化がとらえられてきたが，転座や切断にともなう量的変化の詳細な追求は，まだ十分されてはいない．われわれは量的変化の追求の一つとして，今回は，慢性骨髄性白血病（CML）の臨床像ならびに細胞遺伝学的多様性を検討する意味で，Ph^1 染色体の測定を行った．方法：CML 患者の骨髄および末梢血（PHA 非添加）より，中期分裂像を1症例あたり10個を選択し，黒化度1.2となるように軟調に現像し，このネガフィルムをケンブリッジ社製 QTM-720（テレビカメラ・表示用テレビ・濃度分析機・像修正装置を内蔵）にかけ，G群染色体の個々の濃度を測定した．結果ならびに考察：慢性期20症例の測定より，Ph^1 染色体は相同染色体の53.3～78.3%の大きさに分布しており，症例により，大小のみられることがわかった．また急性転化期8症例では，平均が53.7±4.9%で，慢性期の平均63.5±6.8%と比べて小さい値（$p<0.005$）を示した．2つの Ph^1 を示す症例では，2つの間に大小の認められる例もみられた．また，同一症例で慢性期と急性転化を比較できた症例では，急性転化期の Ph^1 染色体は小さい値を示した．これらは，Ph^1 染色体の大きさと急性転化との関連や，2つの Ph^1 染色体の出現す

る機構について，新しい所見を示すものである．さらに症例数を増やすこと，ならびにDNA量だけの測定方法の検討も必要と思われる．

59. Densitometric Measurements of Fluorescent Intensity of Human Chromosomes Stained by Q-Method: Kazumi TANABE, Toshio SOFUNI and Akio A. AWA (Dept. Clin. Labs., RERF, Hiroshima)

Though human heteromorphic chromosomes have been extensively studied using the Q-staining method, classification of these variant chromosomes is largely based on subjective criteria of the observer. In order to obtain objective data on heteromorphic chromosomes, densitometric measurement of fluorescent intensity of chromosomes by the Q-method was carried out on a total of 100 Hiroshima residents (57 males and 43 females). Metaphases stained by the Q-method were first photographed, and enlarged images of the chromosomes were rephotographed and these negatives were examined by densitometry. Curves corresponding to the fluorescent intensity along the long axis of the chromosome were obtained. For comparative analyses between inter-chromosome regions, only the short arms of the No.13 chromosomes were examined in the present study, and the fluorescent intensity of these short arms was compared to the intense band of the long arm (13q31). Adopting the classification system of the Paris Conference Supplement (1975), four specific bands, 1p36, 9q21, Yq12, and 9q12, selected as indices for classification, were measured by densitometry. Based on these indices, fluorescent intensity was classified into five grades (1: 9q12, 2: 1p36, 3: 9q21, 4: 13q31, 5: Yq12). According to the above classification, 200 No.13 chromosomes were divided into five grades as follows; 1: 1.5%, 2: 24.0%, 3: 45.5%, 4: 23.5%, 5: 5.5%.

60. Quantitative Analysis of C-bands Based on Area Measurement: Toshio SOFUNI, Junso NARUTO and Akio A. AWA (Dept. Clin. Labs., RERF, Hiroshima)

Variation of C-bands of human chromosomes has so far been estimated mainly based on subjective criteria. Only a few attempts have been made to use quantitative approaches to analyzing such variation. We present here preliminary results on quantitative analysis of C-bands based on measurement of area of C-bands in 93 randomly selected Hiroshima residents. One representative metaphase stained by the C-method was photographed for each case and printed an enlargement of about 12,000 fold. The areas of the C-bands in Nos. 1, 9 and 16 chromosomes were measured using a modular system for semiautomatic quantitative evaluation of images (KONTRON, MOP/digiplan). The areas were classified according to the definition proposed by Patil and Lubs (1977): the size of the C-bands was compared to the average area of the short arms of No. 16 chromosomes, and classified into five levels (1: $\leqq 0.5 \times 16p$, 2: $>0.5\text{-}1.0 \times 16p$, 3: $>1.0\text{-}1.5 \times 16p$, 4: $>1.5\text{-}2.0$

×16p, 5:>2.0×16p). According to the above classification, 186 chromosomes each of Nos. 1, 9 and 16 were divided into five levels as follows; *No.1*: 1=4.3%, 2=66.7%, 3=25.8%, 4=2.7%, 5=0.5%, *No.9*: 1=8.1%, 2=85.5%, 3=5.9%, 4=0.5%, 5=0.0%, *No.16*: 1=76.9%, 2=22.6%, 3=0.5%, 4=0.0%, 5=0.0%. These findings indicate that there is considerable variation in the distribution of C-bands in these three chromosomes. Moreover, detailed analysis of the distribution of various levels for the three chromosomes showed that the patterns all approximated "normal distribution," although the means and standard deviation for each were quite different.

61. 血族結婚を有する家系に見られた高度の筋強剛, 四肢軀幹の変形などの錐体外路症状と知能障害を呈する3同胞例： **古賀繁喜・松下兼知・吉牟田直・松下兼介・高橋正名・矢野正敏** (鹿児島県福山町重症心身障害者施設オレンジ学園), **南 道子** (鹿児島大・小児). **A Study of Three Siblings with a Well Marked Extrapyramidal Digidity, Deformities of All Four Limbs and Mental Retardation in a Consanguineous Family:** Shigeki KOGA, Kanemoto MATSUSHITA, Sunao YOSHIMUTA, Kensuke MATSUSHITA, Masana TAKAHASHI, Masatoshi YANO (Orange-Gakuen Hosp. Cerebral Palsy, Fukuyama-cho, Kagoshima) and Michiko MINAMI (Dept. Pediat., Univ., Kagoshima, Kagoshima)

両親が従兄妹結婚であり，3同胞に発症．発端者は31歳の女子．出産正常．新生児黄疸軽度．頸座は2歳．3歳で座る．発語は3～4歳．その後四肢の筋強剛が目立って運動障害，知能発育障害を伴い，19歳ころから臥床状態で経過する．身体発育不良．知能指数39．言語は断節性．深部反射軽度亢進．筋強剛，四肢軀幹の変形が高度である．血液生化学的検査では異常なし．CT-SCANでは前頭葉の軽い萎縮．脳波は low voltage, fast wave. 症例2は，26歳女子．生来寝たきりで，症例1と同様な症状で知能指数は36．症例3は寝たきりで言葉もなく，症状の進行が早く19歳で死亡．このように家族性で乳幼児期に発症し慢性に経過した本症は，従来既知の疾患と比較してかなり態度を異にしており，類似症状を呈する多々ある疾患の中で，病理形態学的に Hallervorden-Spatz 症候群が考えられたが，症例3の剖検所見では，大脳基底核に著変なく，黒質にも鉄反応陽性物質の沈着，Lewy Body は認められず，中枢神経系にも spheroid の存在が認められず，病理組織学的には Hallervorden-Spatz 症候群は否定される．結局，本症例の診断は未確定であるが，遺伝形式は常染色体劣性遺伝と考えられ，慢性の錐体外路疾患として，神経学的に遺伝学的に論議の対象になると考えられる．

62. Inheritance of Nemaline Myopathy Based on Abnormal Tryptophan Metabolism and the Results of Hereditary Analysis of Literature Cases: **Kazuo MIYOSHI, Masatoshi YAGITA, Haruhito NAKAHIRA, Kazuhito KAMEYAMA, Michio TAKUMA, Akira TAIRA, Kanae KUSAKA and Hisaomi KAWAI** (Dept. Int., Tokushima Univ., Tokushima)

An abnormal tryptophan metabolism in the patients of nemaline myopathy and their relatives has been shown by us and this disease was suggested to be transmitted as an X-linked dominant trait (Miyoshi *et al.*: Abnormal tryptophan metabolism in nemaline my-

opathy. 19th Ann. Meeting Jap. Soc. Neurol., 1978). Three probands in three families showed 8.0-17.1 μmole/kg/day of kynurenic acid in the urine in contrast to under 5.0 of controls after loading of L-tryptophan. The mothers of the 3 probands and one grandmother also revealed similar abnormality. Then, the genetic analysis was carried out on 61 reported cases in 37 families including 38 probands. The patients who were confirmed to have nemaline rods histologically in the muscles showed 100% of muscle weakness and atrophy, 71% of high arched palate, 63% of skeletal deformities (vertebrae 50%, thorax 26% and pes cavus 16%). The onset of the symptoms is between 0 and 2 years of age in 80% and before 6 in 95%. The nemaline myopathy patients can be divided into the following four groups according to the age of onset, symptoms and clinical course; 1) severe at birth and will die during infant period, 2) onset before 2 years of age and rapidly progressive, 3) onset after 6 years of age and slowly progressive, and 4) high arched palate and/or skeletal deformities without progression. Among the 38 probands, 24 are isolated, 7 with affected sibling, and 7 with affected parent and/or child. Sex ratio is 23:38, female being nearly 2 times. Seven pairs of affected parent and child showed female to female and female to male transmission, but not male to male. In one family (Gonatas *et al.*), the proband seems to be inherited from father, but the transmission from asymptomatic mother cannot be excluded. In our materials, most of the patients are considered to be transmitted from their mothers, since there is no difference in segregation ratio of sex by sib method. The higher penetrance rate in the siblings (0.29) than the parents (0.18) suggests that only asymptomatic and mild patients can become parents. From these analyses, the nemaline myopathy is considered to be an X-linked dominant trait.

63. Clinico-genetic Study on Spinal Progressive Muscular Atrophies in Infancy and Childfood: Makiko OSAWA, Ekuko OCHIAI, Junko HARADA, Haruko SUZUKI, Yoshito HIRAYAMA and Yukio FUKUYAMA (Dept. Pediat., Tokyo Women's Med. Coll., Tokyo)

The subjects of this study were 101 cases of Werdnig-Hoffmann disease (WH) in 81 families and 11 cases of Kugelberg-Welander disease (KW) in 10 families, who were investigated from 1954 to Nobember 1977. 1) WH cases were classified by the age of onset according to Byers *et al.*, into three types; type I with onset younger than 3 months, 39 cases in 26 families; type II with onset between 3 and 12 months, 37 cases in 32 families; and type III with onset after 1 year, 25 cases in 23 families. 1) WH. Consanguineous marriage among parents was found only in six families. Inbreeding coefficient in the patients was 0.00298. Both sexes were equally affected (M: F=1.1:1). No single parent of the patients was affected. Recurrence was frequent, 17 among 81 sibships. Segregation ratio was 30.95-33.30 in type I, 21.7-25.00 in type II, 8.33-11.11 in type III, and 22.47-25.97 in all families. These values were not significantly deviated from 25% expected from the auto-

somal recessive mode of inheritance, except for type III. The disease type was concordant in all cases of type I. There were four pairs of siblings both affected with type II, two pairs with type II and III, and a pair with type III. The expected value of each of the above three combinations, from the assumption that type II and III are based on the same gene, is 3.57, 2.86 and 0.57 and agreed with the observed valve. 2) KW. No consanguineous marriage was noted. There were two families of which uncle on the maternal side was a patient, and one family, in which both brothers were affected. The proband was a boy in these three families. The male female ratio was 7:4. Segregation ratio was 7.69 ± 7.39. Because of two small number of cases, no definite conclusion could be drawn. From these facts, it is suggested that WH is transmitted by an autosomal recessive mode of inheritance and the gene frequency is relatively high. In KW, from the facts that manifest cases were found in the uncles on the maternal side and affection was noted in both sexes and siblings, sex-linked recessive and autosomal recessive hereditary modes are conceivable.

64. Genetic Patterns of Hereditary Cerebellar Ataxias: Kiyotaro KONDO (Dept. Neurol., Brain Res. Inst., Niigata Univ., Niigata)

Being devoid of pathognomonic abnormalities, genetic analysis of hereditary ataxias is seriously hampered because of poor clinical-pathological correlations, mixed or intermediate cases, different modes of heredity for the same clinical entity, different clinical forms on the same family, *etc.* Within the limitation due to these situations, family patterns of 299 spinocerebellar types, 180 of olivopontocerebellar atrophy (OPCA), 163 of late cortical cerebellar atrophy (LCCA) were analyzed. Spinocerebellar types: This diagnosis merely included cases with predominantly cerebellar ataxia combined with spasticity. Family patterns was not correlated with sex, ruling out sex-linked or sex-influenced inheritances. Parental consanguinity was 18% when the both parents were clinically normal whereas it was unelevated when one of the parents was affected, indicating that the former group included a few recessive cases. The corrected genetic ratio in this group was about 0.25 for cases occurred before 24 years of age. This suggested that younger cases with normal parents involved many recessive cases. Majority of spinocerebellar cases were products of non-consanguineous marriage of which one partner was affected. The segregation ratio was about 0.5 for each decade at onset between 20 and 59, suggesting that most of these cases were dominant. Proportion of these familial cases, however decreased with increasing age at onset, and there were too many sporadics, particularly among elderly cases, to attribute to single-gene heredities. LCCA and OPCA: LCCA shows cerebellar ataxia but no other neurological complications, whereas OPCA various signs including dementia, pyramidal, extrapyramidal, autonomic, *etc.* complicating ataxia. The both

are considered a correlated disease spectrum. Although a weak familial aggregation was observed in the two diseases, autosomal dominant, recessive or X-linked recessive heredities were rejectable. Sib recurrence rate was 7.5% for LCCA, and 9.4% for OPCA. When calculated for different age groups at onset, the rates decreased with increasing age in the two diseases. That is, they were more familial when the ages of onset were younger. Another interesting feature in the two diseases was that the rate increased to 25.0% and 20.0%, respectively given two sib mates already affected, and to 37.5% and 22.2%, given three were affected. These patterns were reminiscent of those in multifactorial diseases.

65. A case of Gingival Fibromatosis with Multiple Hyaline Fibroma (Murry-Puretić Syndrome: Keisuke HAMADA, Shozo OHDO, Kunio HAYAKAWA (Dept. Pediat., Miyazaki Med. Coll., Miyazaki) **and Ichiro KIKUCHI** (Dept. Dermat., Miyazaki Med. Coll., Miyazaki)

A male child of 9 months and 1 year of age with gingival fibromatosis with multiple hyaline fibromas (Murray-Puretič Syndrome) was reported. The parents were consanguineous, but there was no other member like this propositus in the family. Contractures of large joints, hypertrophy of gingiva and tumors and nodules on the body were noted at 4 months, 6 months and 12 months, respectively. Patient's face appearance was mask-like, and mental development was slightly retarded. Routine labolatory examinations disclosed on abnormal findings except hypochromic anemia and hypoproteinemia. No increasing of MPS in urine was noted. Lysosomal enzyme activity in leukocytes was normal. X-ray film examination disclosed thin cortex in all bones and osteolysis of distal phalanges. Histopathologic finding of tumors was proliferation of fibroblast-like tumor cells, which embedded in a homogeneous eosinophilic ground substance with fine fibrous elements. Ground substance was not metachromatic. Electromicroscopic study of tumor cells revealed enlarged vacuoles full of fine granular or fibromatous materials. This very rare disease is considered to be inherited as autosomal recessive trait, but its pathogenesis is not known and a new type of hereditary connective tissue disease is suggested. Study of metabolic dynamics in cultured fibroblast and biochemical analysis of involved tissue are planned.

66. われわれが経験した Mayer-Rokitansky-Küster 症候群について：康　明照・中村徹・阿部洋一・鈴木雅洲（東北大・産婦），**匂坂勝昭**（山形市立病院済生館・産婦）. **Mayer-Rokitansky-Küster Syndrome:** Mei-show KO, Toru NAKAMURA, Yoichi ABE, Masakuni SUZUKI (Dept. Obst. Gynec., Tohoku Univ., Sendai) and Katsuaki SAGISAKA (Yamagata City Hosp. Saiseikan, Yamagata)

Mayer, Rokitansky および Küster らは，膣欠損症の大部分において外陰部および第二次性徴の発育は正常であるが膣欠損と同時に両側痕跡子宮を合併している場合が多いことを指摘し，1961年

Hauser らはこの症候群を初めて Mayer-Rokitansky-Küster 症候群と呼ぶことを提唱した．過去4年間に原発無月経を主訴として当科外来を受診した患者は40名で，そのうち膣形成異常は9例(22.5%)であった．このうち M-R-K 症候群は5例（55.5%）を占めていた．M-R-K 症候群患者の体格と外表については一般正常女性となんら変わるところがない．内分泌的および細胞遺伝学的検査も正常である．この発生原因は，胎生期第7～10週ころに性分化の過程でミューラー管の分化発育が早期停止することにより生じたものと思われる．膣欠損および痕跡子宮にもかかわらず，第二次性徴が正常で基礎体温は二相性を示している．このことは，卵巣機能が正常であることを示す．血液型をみると，膣形成異常では B 型が55.5%，M-R-K 症候群でも B 型が60%の頻度を占めている．本邦における B 型保持者は20%であるから，本症候群では B 型が高頻度を示している．B 型血液と本症との相関関係については，今後の検討を必要とする．1978年 Farber らは本症における術後8年目の患者の rudimentary muscular buds に Lesomyoma が発生したと報告し，また1972年 Duckler らは人工造膣術後の患者で扁平上皮癌または腺癌の発生した症例を報告している．したがって，術後の定期検診は癌の早期発見のためにも必要と思われる．

67. Noonan 症候群の2例：山口正志・城之内浩美・石川　昭（昭和大・医・藤が丘病院・小児）．**Two Cases of Noonan Syndrome:** Masashi YAMAGUCHI, Hiromi JYONOUCHI, Akira ISHIKAWA (Dept. Pediat., Showa Univ., Med. Fujigaoka Hosp., Yokohama)

Noonan 症候群は，Male Turner 症候群，Turner Phenotype などともいわれ，男女両性に発症し，正常の染色体核型を示す家族性遺伝性疾患である．本症候群は，1963年 Noonan 女史らにより先天性心疾患研究中に肺動脈狭窄を呈する9例が短軀，翼状頸，眼球間離間，知能低下，眼瞼下垂，停留睾丸等の Turner 様徴候を共通してもっているのに注目し報告されて以来，Noonan 症候群と呼ばれるようになった．今回われわれは，本症候群と診断した2例を経験した．症例1は，5カ月の男子，家系図には同様疾患はなく散発例と考えられた．頸椎レ線像で第1頸椎と後頭骨の癒合を認め，右母指と第2指の合指をも認めた．症例2は，8歳の男子で，父親が本症候群と考えられ常染色体優性遺伝と考えられた．指趾が短く扁平で，爪の形成不全があり，注腸像にて malrotation が認められた．2症例とも血液，生化学，内分泌検査等でまったく異常なく，免疫学的な検査で液性免疫グロブリンは正常であったが，細胞性免疫とくに T-cell の量的減少が認められた．本症候群では心奇形（とくに肺動脈狭窄）の合併が特徴とされているが，われわれの例では，2例とも右室肥大が示唆されたが，詳細の確認にはいたらなかった．本症と Turner 症候群との鑑別は重要で，染色体検査，心奇形の有無および種類，そして家族内集積性等から判断しなくてはならない．なかでも本症候群の遺伝形成に関しては，諸説（多因子遺伝，常染色体優性，常染色体劣性，伴性劣性遺伝等）があるが，いまだ決定的な説はない．今後本症例の積みかさねによって遺伝形式が解明されていくものと考える．

68. Congenital Diabetes Insipidus in a Family: Shigeru TOMIZAWA, Noriyuki SUETAKE, Osamu KAWANO, Akira MATSUI, Takayoshi KUROUME (Dept. Pediat., Gunma Univ., Gunma) **and Harumi ISHIBASHI** (Dept. Pediat., Tatebayashi Hosp., Gunma)

Patient TS, a 5-year-old male, was admitted to our hospital with a history of polydipsia and polyuria (urine volume in excess of 3 liters/day) since birth. He is the child of con-

sanguineous marriage between the first cousins. His elder brother (patient YS, age 10 years), mother, grandfather, 3 aunts (mother's siblings) and 5 cousins (sons or daughters of 3 aunts) had similar complaints. Both patients and their cousins had a history of slight dehydration or unexplained fevers during their infancy. Psychometric testing revealed low intellectual function in TS and normal function in YS. By physical examination, TS proved to be a relatively small boy with scoliosis, however YS was normal except for obesity. Roentgenographic examination of genitourinary system by intravenous pyelography showed staghorn calculus without excretion of contrast medium in right side kidney of TS and showed low contrast density in pelvis and ureter with caliectasis in YS. Cystogram revealed a massive dilation of bladder in both patients, with reflux in TS. Echo- and Renogram revealed a small contracted kidney without function at right side in TS. None of the patients, their mother, an aunt and 2 cousins were able to concentrate their urine. By water loading tests in both patients, the urine specific gravity and urine osmolality did not rise above 1,007, 175 mOsm/L respectively. However, after pitressin injections, urine specific gravity and osmolality rose up to some degree with about 2-fold increases in urinary cyclic AMP excretion, though urine concentration was not greater than that of plasma. Plasma ADH levels in both patients and mother had normal values. Renal biopsy performed in both patients were interpreted as minimal changes by light microscopy. From these findings, it was suggested that the diagnosis of these patients might be a "partial" form of congenital nephrogenic diabetes insipidus.

69. 軟骨形成不全症の臨床遺伝学的検討：勝田隆子・石飛和幸・渡辺 章・仲田教子・二宮哲博・原田義道（鳥取大・三内）. **Clinical Studies of 46 Cases with Achondroplasia:** Takako KATSUTA, Kazuyuki ISHITOBI, Akira WATANABE, Noriko NAKATA, Tetsuhiro NINOMIYA and Yoshimichi HARADA (3rd Dept. Med., Tottori Univ., Yonago)

低身長を主訴として来院した Achondroplasia 46例（男24例，女22例）における家族的背景，両親，同胞の年齢，身長，患者出生時の状況から現在までの身体発育経過等につき追跡調査した．また，骨とくに骨盤，脊椎のレ線学的所見，脳波，IQ，内分泌機能検査所見等についても検討した．6家系8例（いずれも男子）が家族性で，父とその子供の兄弟に本症を認めたものが2家系，父と子供1人が1家系，母と子供1人が1家系，兄弟2人が1家系，不明1家系であった．両親の血族結婚は34家系中4家系にみられ，いずれもいとこ結婚であった．同胞数は平均23人，出生順位は平均1.8で，家族性のあるものを除外して症例の出生時の両親の年齢は，父33.2±4.5歳，母28.4±4.2歳で，父の高年齢の傾向がみられた．分娩は，頭位23例，骨盤位6例，帝王切開3例であった．在胎週数は男39.9±0.9週，女39.3±1.2週，生下時体重男3.2±0.4 kg，女2.9±0.5 kg，身長男48.4±2.6 cm，女47.3±2.4 cm，頭囲男34.6±1.9 cm，女35.0±3.0 cm，歩行開始年齢は平均18.9カ月と著明に遅延した．初診時年齢は11カ月から13歳にわたり，身長は平均男-4.6σ，女-4.9σ，最終身長の平均は134.6±9.1 cm であった．IQ は104.5±18，脳波異常は26例中11例（42.3%）にみられた．内分泌機能検査所見はいずれも正常であった．骨盤および脊椎のレ線学的所見を男24例，女19例につき-2σ以内の

正常短軀者を対照として検討した．腸骨最大縦経が小さく，腸骨最大横経が大であり，腸骨下半高の有意な短縮，腰椎椎弓根間距離の狭少化が下部腰椎ほど著明であった．

70. Short Rib-Polydactyly Syndrome, Majewski Type (Majewski Syndrome) in Two Sibs: Tomiko MOTEGI, Masako KUSUNOKI, Takeshi NISHI (Dept. Pediat., Tokyo Univ. Branch Hosp., Tokyo), **Tetsuro HAMADA, Nobuko SATO** (Dept. Obst. Gynec., ditto), **Tetsuo IMAMURA and Noboru MOHRI** (Lab. Pathol., ditto)

Two sibs with Short rib-polydactyly syndrome, Majewski type are described. The present report may be the first one of sibs, confirmed clinically, radiologically and pathologically. The first male sib was born at 37 weeks' gestation by cesarean section, following a pregnancy complicated with hydramnios. Birthweight was 3,150 g, length 45 cm, head circumference 36 cm, chest circumference 27 cm and span 37 cm. Apgar score was 8 just after birth, but respiratory insufficiency rapidly progressed and died at 11 hr old. Abnormal clinical findings included the disproportionate shortness of extremities with the legs especially shortened, flat nasal bridge, low-set malformed ears, median cleft lip, narrow thorax, protuberant abdomen, ambiguous genitalia and polysyndactyly (8 digits on each of the right extremities and 7 digits on each of the left extremities). There were total syndactyly of 1st and 2nd fingers, bilaterally, and 1st, 2nd and 3rd toes, bilaterally. Radiologic findings showed the short and horizontal ribs with enlargement of the chondro-osseous border, marked shortening of tibias and the premature appearance of the secondary ossification center of the femoral head. Pathologic abnormalities were phyoplasia of the epiglottis and larynx, small and atelectatic lungs, multiple glomerular cysts of the kidney and the anomaly of the genitalia including high-degreed hypospadias, rudimentary vagina, cryptorchidism and moderate-degreed hypoplasia of testes. Long bones (humerus, femur and tibia) and vertebrae showed abnormal endochondral ossification which exhibited the shortening of the physeal growth zone with rather irregular and poor alignment of the chondrocytes. These changes were maximum in the tibia and minimal in the vertebra. The second male sib was born 3 years 3 months later, following a pregnancy of 37 weeks which was complicated with hydramnios. Apgar score was 3 just after birth and died at 25 hr old. Birthweight was 2,410 g, length 42 cm, head circumference 35 cm, chest circumference 24 cm and span 35 cm. Clinical, radiological and pathological findings showed the similar changes to the older sib except no premature ossification of the femoral head and the details of polysyndactyly. He had 8 fingers on the right hand and 7 digits on each of the other extremities. Total syndactyly of the 1st and 2nd digits on each of the upper and lower extremities, bilaterally, and partial syndactyly of the 4th and 5th, and 6th and 7th on the right hand, and 3rd and 4th on the right foot were noted. To our knowledge, there were seven cases confirmed as Majewski syndrome including our own

two cases; three males, three females and the other one unknown sex. The data mentioned above indicate no difference in both sexes. This family provided the evidence that Majewski syndrome is a genetic disease, probably with an autosomal recessive inheritance.

71. **Genetic Study on Lethal Short-limbed Dwarfism:** Yasuo SUGIURA (Dept. Orthop. Surg., Nagoya Univ., Nagoya) **and** Toyoshi TSURUTA (Dept. Orthop. Surg., Mie Univ., Tsu)

We are reporting 41 original cases of lethal short-limbed dwarfism studied in the last 6 years. Among them, 5 cases were achondrogenesis of which two were siblings born to normal parents. This fact indicates the autosomal recessive mode of inheritance like other reported cases. Thanatophoric dysplasia (formerly thanatophoric dwarfism) was found in 7 cases. Though over one hundred cases have been reported in the world, no intrafamilial occurrence was showed. Therefore, the genetics of this disease is still unknown. The congenital lethal form of hypophosphatasia was found in 6 caces. The autosomal recessive inheritance has been clarified by other workers. As in the parents of the present 2 cases serum alkaline phosphatase was abnormally low, they were considered to be heterozygous for this gene. The congenital lethal form of osteogenesis imperfect is considered to be autosomal recessive. This form was found in 11 cases. Two of them were siblings born to normal parents. The Saldino-Noonan type of short rib-polydactyly syndrome was observed in 1 case. The mode of inheritance of this disease has been considered to be autosomal recessive. The Majewski type of this disease was 3 cases. The genetics of this disease was unknown. However, the sibling cases born to normal parents, which were reported by Motegi *et al.* in this meeting, strongly suggest the autosomal recessive mode of inheritance. Chondrodysplasia punctata was classified by Spranger *et al.* into 2 types; Conradi-Hünnermann type and recessive rhizomelic type. We found each one case. The latter is lethal and the mode of inheritance is autosomal recessive. The remaining 7 cases of lethal short-limbed dwarfism have not yet been identified. These results are available for genetic counseling.

72. **家族性大腸ポリポーシスの臨床遺伝学的研究：発癌年齢の近親間相関：宇都宮譲二**（東医歯大・医・二外），**谷村雅子・岩間毅夫**（同ポリポーシスセンター），**田中克己**（同難研・人類遺伝），**外村 晶**（同細胞遺伝）. **Clinical Genetic Study of Familial Polyposis Coli: Correlation of the Age at Onset of Cancer between Relatives:** Joji UTSUNOMIYA (Dept. 2nd Surg., Tokyo Med. Dent. Univ., Tokyo), K Masako TANIMURA, Takeo IWAMA (Polyposis Center, Tokyo Med. Dent. Univ., Tokyo), Katsumi TANAKA (Dept. Hum. Genet., Tokyo Med. Dent. Univ., Tokyo) and Akira TONOMURA (Dept. Cytogenet., Tokyo Med. Dent. Univ., Tokyo)

ポリポーシスセンターに登録されている大腸腺腫症患者の306家系の家系調査結果に基づき，本症

患者の発癌年齢の異質性について遺伝学的見地から分析を行った．大腸癌を伴う本症患者の診断時年齢分布は，男子は30歳および40歳前後に，女子は20歳前半および30歳前半におのおの２つのモードがあり，癌の発生に早発型・遅発型の存在が示唆された．患者の死亡年齢の近親間相関係数は，同胞では兄弟 0.64**，姉妹 0.52**，兄妹 0.38，姉弟 0.40* と相関性があり，とくに同性同胞は異性同胞より高い傾向にある．親子間では母娘0.32以外は低い値であったが，これは親世代には生殖年齢前に死亡したものが除去されているためとも考えられる．このような影響のないおじおい間では0.37，おばめい0.28，おじめい0.16，おばおじ0.19で，多少とも相関がみられた．このように死亡年齢おそらくは癌の発生年齢に同胞間のみでなく近親間に相関があることから遺伝的要因の関与が考えられる．本症には腺腫の多い例（密生型）と比較的少ない例（非密生型）とが存在する．密生型家系の患者は30～40歳で多く死亡するが，非密生型では早く死亡するものもいるが50％は45歳以降であることがわかった．家系調査の結果より密生・非密生は主遺伝子の異質性によると考えられるので，癌発生の早発・遅発もこの異質性が関与している可能性が示唆された．

73. 発がん遺伝子に対する宿主抵抗性：松永　英（国立遺伝研）．**Inherited Host Resistance to the Gene for Retinoblastoma:** Ei MATSUNAGA (Nat. Inst. Genet., Mishima)

網膜芽細胞腫の約60％は非遺伝性（常に片眼性）であるが，残り40％は遺伝性で，その大多数は健康な親の配偶子に生じた優性突然変異による．この突然変異遺伝子の保因者の表現型には，外見上正常なもの，片眼罹患および両眼罹患のものがある．このような表現度の違いは，主遺伝子に対する宿主の遺伝的抵抗性の違いによると考えられる．家族性に網膜芽細胞腫の出ている231組の同胞群を文献から集めて分析すると，子の罹患率と表現度は，保因者である親の表現度に応じて変動する．例えば片親が両眼罹患の場合には，子どもの49％が発病しその90％が両眼性であるが，片親が健康な保因者のときには，子どもの罹患率は31％に下がり両眼罹患率も54％になる．滲透率の変動は同一家系内の同胞間にも見られるから，主遺伝子座に表現度の異なる突然変異遺伝子が幾種類か存在する可能性は排除される．上の数値に基づいて，主遺伝子を受けた子集団での各表現型の分布を求めることができる．外見上正常のもの，片眼性および両眼性罹患のものの割合をそれぞれ c, u, b (c+u+b=1) とすると，例えば健康な保因者の親から遺伝子を受けた子集団では c=0.38, u=0.28, b=0.34 となる．もし Knudson (1971) の想定するように腫瘍形成が（宿主抵抗性に関係なく）Poisson 分布に従うとすると，$u^2=4cb$ が成立するはずであるが，親の表現度によって分類される３種類の子集団での実測値は，いずれもこの期待から大きくずれている．一方，宿主抵抗性が正規分布し，二重のしきいによって各表現型が分けられると仮定すると，標準偏差で測ったしきい間の距離は0.6～0.9となり，３種類の子集団の間で大差ない．宿主抵抗性の遺伝率は約90％と推定された．詳細は *Am. J. Hum. Genet.* **30**: 406–425, 1978 に発表．

74. 全身性エリテマトーデス (SLE) の家族および集団研究（第1報）：梶山憲治，自見庄三郎，草場公宏，木須達郎，亀田志郎，児玉武利，山口雅也，柳瀬敏幸（九大・一内）. **Family and Population Studies of Systemic Lupus Erythematosus:** Kenji KAJIYAMA, Shozaburo JIMI, Tomohiro KUSABA, Tatsuro KISU, Shiro KAMEDA, Taketoshi KODAMA, Masaya YAMAGUCHI and Toshiyuki YANASE (1st Dept. Med., Univ. Kyushu, Fukuoka)

1975年～1977年に福岡市在住で ARA 診断基準による確実 SLE の罹患者は108名（調査回収率92%）で，最低有病率は108×10^{-6}である．このうち女性は103名で，10歳以上の女性集団における有病率 (P) は264×10^{-6}である．一方，北部九州における95名の女性発端者の第1度の近親で6家系6名（母娘，姉妹それぞれ3例）に SLE 再現があり，10歳以上の女性における同胞罹患率2.19%(3/137) の P に対する比は，SLE がポリジーン形質であると仮定した場合の期待値に近い．両親のいとこ結婚率は3%であった．SLE の近親では抗核抗体，リウマチ因子，梅毒の生物学的疑陽性や抗甲状腺抗体などの頻度および IgG, A, E などの高値をもつ個体の頻度が対照健康人家族に比し高かった．IgE 濃度の健康人における分布は IgG, A, M と同様にほぼ正規分布であった．親子相関は 0.27 ($N=134$, $p<0.005$)，同胞相関は 0.39 (N 81, $p<0.001$)，夫婦相関は 0.23 ($N=29$) で IgE 量に対する狭義の遺伝力は0.54となり，IgA, M と同程度であった．一方，SLE の近親では IgE 量の平均値が IgG, A と同様に男女とも健康人家族より有意に高く ($p<0.001$, $p<0.005$) また IgG, A, M にはみられない同胞相関が 0.48 ($N=41$, $p<0.005$) と高い点が注目された．SLE 発端者と近親の補体・免疫グロブリンなどの変異体の screening を進めているが，発端者とその姉に補体の著明に低下している1家系などが発見され，SLE 発症に免疫系の突然変異がかなり重要な役割を果たす可能性が示唆される．

75. Plasma and Urine Uric Acid Levels in Twins and Their Parents: K.S. Park, E. Inouye and A. Asaka (Inst. Brain Res., Univ. Tokyo, Tokyo)

Plasma and urine uric acid levels were measured in 17 families, each consisting of twins (aged 11 and 12 years) and parents, by Boehringer-Mannheim uricase test (OD at 410 nm and using 6 mg/100 ml standard solution). After correction for age separately for males and females the value x was standardized by $X=(x-\bar{x})/\sigma$ again separately for two sexes, and X was subjected to genetic analysis. Correlations or regressions of plasma uric acid level were: parent-offspring regression (b_{po})=.5452 ($N=54$), mid-parent-offspring regression ($b_{\bar{p}o}$)=.8415 ($N=24$), MZ twin correlation (r_{mm})=.8536 ($N=13$), and husband-wife correlation (r_{hw})=.5119 ($N=13$). Since total variance is taken unity, expectations are $b_{po}=(1+\rho)V_A/2+V_{EC}$, $b_{\bar{p}o}=2(V_A/2+V_{EC})$, $r_{mm}=V_A+V_D+V_{EC}$, and $r_{hw}=\rho+V_{EC}$ (V_A: additive variance, V_D: dominance variance, V_{EC}: variance due to common environment within family, ρ: phenotypic correlation of husband and wife at mating). These simple models permitted to estimate variance components and ρ; $V_A=.6201$, $V_D=.1227$, $V_{EC}=.1107$, $\rho=.4012$. The result indicates a high heritability and positive assortative mating. Analysis of the urine uric acid level indicated the same magnitude of

ρ(.4288), negligible V_D and V_{EC}, and low V_A(.3700). The significance and implications of the above findings were discussed.

76. Similarity of Three-dimensional Tooth Morphology in Twins: Minoru NAKATA

(Dept. Pedodont., Tokyo Med. Dent. Univ., Tokyo)

Genetic studies on tooth have been based on single measurements such as mesio-distal or bucco-lingual diameters, or subjective assessments of occlusal pattern, despite the fact that the shape of tooth itself is three-dimensional. The objectives of the present study are to analyze the dental character by the three-dimensional measurements and to detect genetic contribution to the morphology of tooth by twin method.

Samples: The dental casts of 53 sets of like-sexes twins (39 monozygotic twin pairs and 14 dizygotic twin pairs) were selected, and duplicate measurements, right and left comparison within individuals, and unrelated pairs were obtained from these twin materials.

Methods: On the dental casts, 10 anatomical points of cusps, pits and fissures were selected for the upper 1st molar and 13 points for the lower 1st molar. A computer-based three-dimensional recording system was utilized for measuring the co-ordinates along the X, Y, Z axis for each point on the detal casts. The overall similarity between the two teeth in three-dimensional space was obtained by fitting one to the other, as follows: The original values of the co-ordinates are symbolized as X, Y, and Z. Tooth sizes were brought to the same size by standardizing the two sets of data in terms of standard deviation, where the standard deviation (s_{XYZ}) is the standard deviation about the $\bar{X}$, $\bar{Y}$, and $\bar{Z}$ point,

$$s_{XYZ}=\sqrt{\frac{\sum X^2}{h}+\frac{\sum Y^2}{h}+\frac{\sum Z^2}{h}-\bar{X}^2-\bar{Y}^2-\bar{Z}^2}$$

where h is the number of points.

$$x=(X-\bar{X})/s_{XYZ},\ y=(Y-\bar{Y})/s_{xyz},\ z=(Z-\bar{Z})/s_{XYZ}$$

The standardized values, symbolized as x, y, and z were used to obtain the overall similarity of three-dimensional shape between the two teeth, A and B, after the superimposition of one to the other. The d_h, root mean square h-pair distance at best possible fit is,

$$d_h=\sqrt{\sum((x_A-x_B)^2+(y_A-y_B)^2+(z_A-z_B)^2/h}.$$

Results: Intra-class correlation coefficients for tooth size (s_{XYZ}) were r_{MZ}=.717 (n=37) and r_{DZ}=.491 (n=14) in upper 1st molar and r_{MZ}=.683 (n=39) and r_{DZ}=.568 (n=14) in lower 1st molar. The values of three-dimensional similarity after standardizing for tooth size were d_h=.099±.028 for MZ twins and d_h=.125±.028 for DZ twins in upper 1st molar, and d_h=.097±.028 for MZ twins and d_h=.125±.028 for DZ twins in lower 1st molar. It was shown that the three-dimensional contour of tooth was determined by genetic factors as well as tooth size.

77. **Segregation Analysis of Blindness: Norikazu YASUDA** (Div. Genet., Nat. Inst. Radiol. Sci., Chiba), **Akira NAKAJIMA, Utako TANABE** (Dept. Ophthal., Juntendo Univ., Tokyo), **Kazuyuki KABASAWA** (Computer Center, 2nd Dept. Physiol., Juntendo Univ., Tokyo) **and Keiko FUJIKI** (Dept. Opthal., Juntendo Univ., Tokyo)

Analyzing the data of ab. 15,000 blind persons at blind schools, we already have obtained the detrimental equivalents of visually handicapped in the Japanese population and have genetically analyzed each eye disease. In this report, the inbreeding and segregation analyses of all data of blindness were tried. Probability of ascertainment (π) was 0.47 in all cases of blindness and changed from 0.14 to 0.70 by the year of birth of the blind. Proportion of the sporadic cases (x) was 0.64 ± 0.01 and did not change by the year of birth. Prevalence of blindness was estimated to be 4.5×10^{-4} from the cases of the blind who were born during 1946–1950; 3.9×10^{-4}, during 1951–1955; and 3.4×10^{-4}, during 1956–1960. The trend of decrease in these values nearly coincides with the decrease of blindness under 19 years old in the Japanese population. On the heterogeneity of blindness, the autosomal recessive and dominant inheritance and others were estimated to be 36, 27 and 37 per cent, respectively. The mutation rates of the autosomal recessive and dominant estimated by the data of the year of birth during 1951–1960 were $(4.8\text{–}8.8)\times10^{-5}$ and $(1.8\text{–}3.3)\times10^{-5}$. respectively. Although the ratios of the recessive inheritance in blindness, estimated every five years during 1910 to 1960, were compared with each other, they have hardly changed. This fact seems to show that the effect of the decrease of the consanguineous marriages among recently Japanese population does not yet extent to this data.

78. **人類遺伝学研究のための光学読取カードの設計と入力プログラムの開発：東 晨児・林 健児**（東理大・理），**工藤昭夫**（九大・理）. **Design of Optical Mark Card and Input Program for Human Genetics Study: S. AZUMA, K. HAYASHI** (Tokyo Sci. Univ., Tokyo) and A. KUDÔ (Kyushu Univ., Fukuoka)

人類遺伝のデータを計算機に入力する媒体としての光学読取カードの利用は，つぎのような利点が考えられる．1）資料整理の効率化．2）個人秘の保護と医師と情報処理技術者との分業．3）プログラムでロジカルチェックが可能．4）単純な図形の入力媒体として利用可能．

われわれは，誤記入を発見するプログラムを開発し，人類遺伝のデータを利用して実験を行った結果，60～80%の誤記入を発見することができた．また，戸籍収集を終了し現存の夫婦の子と直系祖先を記入した資料を用いる隔離集団専用のカードを試作し，記入実験を行った．隔離集団のデータの特徴は，重複して記入された個体を決定しなければならないことであるが，近親結婚が多いので容易に判明する場合が多い．われわれの実験では，記入時に判明したもの 2/3，記入後計算機の助けによって判明したもの 1/3 である．1,432 個体のうち 1 回だけ現れた個体数は 871，最も多く現れたのは 96 回（1 個体），次は 47 回（2 個体）であった．誤記入のチェックの成績は，一般の場合とほぼ同様である．隔離集団については実験が続行中である．

79. The Secondary Sex Ratio, Paternal Age, Maternal Age, and Birth Order in Japan:
Yoko IMAIZUMI (Inst. Popul. Prob., Tokyo) **and Motoi MURATA** (Nat. Inst. Rad. Sci., Chiba)

Human secondary sex ratio may still now be conceived a useful tool for inspecting genetic damage due to ionizing radiation. Many biological and social factors are related to its variation among different populations. After the report of Takahashi (1954), no one has investigated this problem with Japanese data. The present study is composed of two parts, that is an analysis on the simultaneous effect of paternal age, maternal age and birth order, and that on the chronological change of sex ratio. First, using birth certificate records of over 3.7 million live births in Japan during 1975-1976, a multiple regression analysis on the effects of paternal age (9 classes PA), maternal age (7 classes MA) and birth order (6 classes BO) was carried out with both linear and quadratic models. Here the sex ratio is defined as the proportion (p) of male among total births. With the linear model ($p=b_0+b_1(PA)+b_2(MA)+b_3(BO)$), partial regression coefficient (b) is estimated to be $-.00008\pm.00038$ for PA, $.00029\pm.00045$ for MA and $-.00020\pm.00037$ for BO, respectively. With the quadratic model ($p=b_0+b_1(PA)+b_2(MA)+b_3(BO)+b_{11}(PA)^2+b_{22}(MA)^2+b_{33}(BO)^2+b_{12}(PA)(MA)+b_{13}(PA)(BO)+b_{23}(MA)(BO)$), positive b for PA, $(MA)^2$ and (PA)(BO) and negative b for $(PA)^2$, $(BO)^2$ and (PA)(MA) were obtained. These values are all not statistically significant. The latter model is relatively more powerful than the linear model in explaining the sex ratio variability. Statistical non-significance is probably due to the narrower range in parental ages and parity in the present material compared with that in foreign countries. However at least the negative association of birth order with the sex ratio is conformed among them. When the same material is classified by the occupation of parent (6 classes), effect of birth order is consistent but that of maternal age is quite variable among classes. For the second analysis, vital statistics on the sex ratio of 55 million live births during the period of 1947–1976 except 1950 were used. Sex ratio gradually increases with time and simple regression coefficient is $.00011\pm.00001$ ($p<.001$). After pooling the data of the whole years, multiple regression analysis with two variables (MA and BO) was performed. Value of b is $.00019\pm.00012$ for MA and $-.00032\pm.00009$ for BO, the latter being statistically significant ($p<.001$). These data are classified into 6 quinquennial period groups and again analysed. Association of the two variables, especially MA, with the sex ratio is quite inconsistent among year groups. These results indicate that factors other than these are also related to the human sex ratio in a interacting way.

80. 無脳症発生率と父年齢，母年齢および出産順位との関係について： **今泉洋子**（厚生省人口問題研究所）． **Anencephaly in Japan: Paternal Age, Maternal Age and Birth Order:** Yoko IMAIZUMI (Inst. Popul. Prob., Tokyo)

日本全国において，1975年および1976年の2年間に無脳症で死産した1,815件の死産票および同一期間に日本全国で出生および死産した者，約394万人の出生票および死産票をもちいて，無脳症発生率におよぼす父年齢，母年齢および出産順位の影響を多変量解析法により調べた．その結果，無脳症発生率におよぼす父年齢 (PA)，母年齢 (MA)，出産順位 (BO) の影響を単純（直線）回帰モデルで分析したところ，統計的有意差をもって出産順位の影響が大きいことが判明した．次に，無脳症発生率におよぼす要因として，上記3要因の一次の項 (PA, MA, BO)，二次の項 (PA^2, MA^2, BO^2) および相交作用の項 (PA×MA, PA×BO, MA×BO) の影響を二次回帰モデルにより分析したところ，統計的有意差をもって BO^2（正），PA×BO（負），MA×BO（負）の効果が認められた．重回帰係数は直線回帰モデルの場合0.24，二次回帰モデルの場合 0.61 を示した．したがって二次回帰モデルの方が直線回帰モデルよりも適合したモデルであることが判明した．

81. 原爆被曝者の孫の性比：古庄敏行（鹿児島大・衛生）．**Sex Ratio in the Grandchildren of Atomic Bomb Survivors:** Toshiyuki FURUSHO (Dept. Hyg., Kagoshima Univ., Kagoshima)

放射線によるヒトのX連鎖劣性致死突然変異の検出は，孫の性比の変動からも推定できる．すなわち，被曝者（父のみ被曝群，母のみ被曝群および両親とも被曝群）の (a) 娘の男児，(b) 娘の女児，(c) 息子の男児，(d) 息子の女児について調査し，娘の子の性比 m_1 を同一群の息子の性比 m_2 あるいは非被曝群の性比 m_0 と比較すると，$m_1<m_2\simeq m_0$ の関係が期待される．広島資料について，父のみ被曝群，母のみ被曝群および両親とも被曝群の m_1 は，0.4935, 0.4844, および 0.4844 で同一群の m_2 は，0.5526, 0.4672, 0.5102, また非被曝群の m_0 は，0.4997～0.5170 で，母のみ被曝群の場合のみ $m_1>m_2$ で遺伝仮説に合わないが，非被曝群の m_0 と比べると $m_1<m_0$ で合致する．また被曝群をまとめて性比を計算すると $m_1=0.4951$, $m_2=0.4863$ で遺伝仮説に合致する．しかし，いずれも m_1 と m_2 または m_0 との間の差は統計的有意水準に達しなかった．

82. Spontaneous Abortion Risks in Mothers of Human Embryos with Cleft Lip: **Kohei SHIOTA** (Dept. Anat., Kyoto Univ., Kyoto)

It has been reported that the frequency of spontaneous abortions in sibships and other family members of propositi with cleft lip (CL) and/or cleft palate (CP) is less than in control families without CL and/or CP patients (Warburton and Fraser, 1964; Henricksson, 1971; Bear, 1973). Since the occurrence of such malformations as anencephaly and club foot is usually associated with increased abortions in the families, spontaneous abortion risks in mothers of embryos with CL(P) were examined using the reproductive data from the collection of human embryos in the Congenital Anomaly Research Center, Kyoto University. Fourteen out of the 37 mothers (37.8%) of the CL(P) embryos had experienced one or more spontaneous abortions. The frequency of spontaneous abortions was

19.8% (22 abortions in 111 recognized pregnancies) and was significantly ($p<0.01$) higher than the corresponding figure in parity-matched normal controls (4.5%; 10/222). Spontaneous abortions were more frequent in mothers of embryos with bilateral CL than in those with unilateral one. These findings together with the low abortion frequency in families of CL(P) "patients" indicate that there may exist variation in the risk of being selected by spontaneous abortion among early intrauterine population of CL(P) embryos. It can be assumed that many of the recurrent cases of CL(P) would be eliminated early in their intrauterine life and that the embryos with low abortion risks might escape spontaneous abortion and survive to birth. Comparative data on newborn CL(P) cases are required to test this hypothesis.

83. 糖原病24例の病型に関する研究：大和田操・北川照男（日大・小児）. **Genetic Types in Twenty Four Cases of Glycogen Storage Disease:** Misao OWADA and Teruo KITAGAWA (Dept. Pediat., Nihon Univ., Tokyo)

糖原病は肝型，全身型，筋型に大別され，肝型の頻度が最も多く，わが国でもその研究は稀ではないが，肝型糖原病のおのおのの病型の頻度については未だ不明な点が多い．われわれは，過去7年間に24例の糖原病を経験したが，その内訳は肝型22例，全身型2例であった．肝型糖原病の22例について，下記に述べる方法で病型分析を行い，各病型のわが国における頻度について検討した．方法：1) 一般検査として，空腹時血糖，血中乳酸，血清triglyceride，血清尿酸を，2) 負荷試験として glucose, galactose, glucagon 負荷試験を，3) 血球の分析として赤血球 glycogen 量，白血球 debranching enzyme, phosphorylase の測定を，4) 肝組織における glycogen 定量，G6Pase, debranching enzyme, phosphorylase 活性測定および肝の病理組織学的検索を行った．結果：22例中11例 (50%) はⅠ型，5例 (23%) はⅢ型，3例 (11%) はⅥ型あるいはⅧ型であり，残りの3例 (11%) は病型不明であった．考察：肝型糖原病の病型別頻度は各国において異なり，オランダ，フランス，ノルウェーなどでは圧倒的にⅢ型の報告が多く，U.S.A. では，Ⅰ, Ⅲ, Ⅵ がおのおの1/3ずつを占めているといわれている．わが国では1934～1964年の報告の集計（垂井ら）では，89例中99%がⅠ型と報告され，1965～1972年の集計（合屋ら）では103例中74%がⅠ型と報告されている．しかし，過去の報告では病型診断は臨床診断によるものが多く，生化学的診断法の普及によって，従来臨床的にⅠ型と診断されていたものが，他の病型であることが明らかになったものが少なくない．そこで，われわれは生化学的診断による病型分析を行い，その病型別頻度を研究したが，やはり本邦ではⅠ型が比較的多く，次いでⅢ型が多かった．最近，Ⅸ と分類されていた症例の一次的な障害が明らかにされたが，病型診断法の進歩によって，肝型糖原病はさらに細かい subtype に分類される可能性もある．

84. Adenosine Deaminase Deficiency Disease: The First Family in Japan: Shigeru TSUCHIYA, Nobuhiro ARAI, Masafumi KUDO, Kuniaki NARISAWA, Tasuke KONNO and Keiya TADA (Dept. Pediat., Tohoku Univ., Sendai)

A patient (a 15 month-old male infant) with severe combined immunodeficiency with adenosine deaminase (ADA) deficiency, the first case in Japan, was reported. Two sisters

of the patient died of a similar illness at the age of 1 year. ADA activities in the red blood cells from the family members examined showed that the mother (15.3), father (31.3), maternal uncle (19.5) and maternal grandmother (31.3) were presumed carriers (control subjects, 69.6±16.6 nmoles/mg Hb/hr; n=16). ADA activity in the lymphoblastoid cells (LC) established by Epstein-Barr virus from the patient and parents were also examined. ADA activity in LC from the patient was below the detectable level. ADA activities in LC from the mother (4.94) and father (3.41) showed approximately a half level of control subjects (8.03±3.88 μmoles/mg protein/hr, n=7). No inhibitor against ADA activities were found in the lysate from the patient's LC.

85. 先天性高ビリルビン血症の遺伝的異質性. II) 各種ビリルビン抱合体の高速液体クロマトによる分離, 構造決定, および生理的意義： **山口登喜夫・山口信子・溝田悦子・中島 熙**（東医歯大・難研），**瓶田泰夫・石川正幸**（同・医用研）

（抄録なし）

86. 先天性高ビリルビン血症の遺伝的異質性. III) Gilbert 症候群および Dubin-Johnson 症候群患者の血清および胆汁中ビリルビン抱合体： **山口登喜夫・山口信子・中島熙**（東医歯大・難研），**近藤俊文**（宇和島病院・内科），**口羽和雄**（津島中央病院・外科）

（抄録なし）

87. Color Blindness and Hereditary Persistence of Fetal Hemoglobin (Tokushima Type): **Kazuo MIYOSHI, Naoko SASAKI, Shinji NIKI, Yoshikado KANETO, Kimiaki MANABE and Hisaomi KAWAI** (Dept. Int. Med., Tokushima Univ., Tokushima)

A new type of hereditary persistence of fetal hemoglobin, HPFH (Tokushima type) which is inherited as an X-linked dominant trait, was initially found in Japanese healthy adults in our clinic (Miyoshi *et al.*, *IGAKU NO AYUMI* **103**:146, 1977 and *J. Jap. Soc. Intern. Med.* **67**: 1068, 1978). The incidence of this HPFH was 10% in male and 19% in female Japanese. The percentage of erythrocytes containing HbF (F-cells) is 4.5–14.1% in contrast to 0.3–4.3% of non HPFH. This type of HPFH might be found in the world as well as in Japan. We studied the linkage between the gene of color blindness which is located on X chromosome and that of this type of HPFH. Seven cases in 51 patients with color blindness were found to have HPFH. The incidence was 13% and roughly coincided with that of HPFH in healthy males. In 2 families, the combination of color blindness and HPFH (Tokushima type) was studied. 1) Ha. family: Four members, the proband, his elder brother, a daughter of the brother and a cousin, were concordant with color blind-

ness and HPFH. A son of elder sister of the proband had color blindness and non-HPFH. Other two elder brothers and two cousins of the proband were neither color blindness nor HPFH. In this family, genes of color blindness and HPFH were concordant in 8 members and discordant in one. 2) Yo. family: The proband had both color blindness and HPFH, but his brother had color blindness and non-HPFH. In these 2 families, 9 members were concordant in color blindness and HPFH and 2 members were discordant. The recombination value between the genes of color blindness and HPFH (Tokushima type) was 18%. It is suggested that the loci of both genes on X chromosome are relatively close.

88. Biochemical Diagnosis of Hereditary Disorders by Use of Hair Follicles: Zen-ichi OGITA, Ken-ichi YAMAMURA, Namiko KITAHARA and Hidetaro YASUMITSU (Dept. Biochem. Pathol., Inst. Oriental Medicines, Toyama Med. Pharmaceut. Univ., Toyama)

The application of the human scalp hair follicle as a diagnostic sample to the detection of heterozygotes which have an X-linked hereditary disorder, has increased the utilization of biochemical tests (Gartler *et al.*, 1969, 1971; Goldstein *et al.*, 1971; Ogita *et al.*, 1976). Cytogenetic and biochemical examinations to monitor inborn errors of metabolism in hair follicles have raised a question whether the cells should be cultured or not. Uncultured cells have obvious advantages that ultra microassays can be performed effectively in a matter of hours rather than a delay of weeks. The examination of hair follicles has the following difficulties. 1) Contamination by fungi and bacteria. 2) The apparent heterogeneity of hair follicle cells in the outer root sheath and bulb. 3) The procedure of extraction of enzymes and proteins from the single hair follicle. 4) Methods of quantitative microassays for enzyme and proteins. Improved techniques have solved these problems. One of them is the miniaturized slab gel electrophoresis on polyacrylamide gel (Ogita and Markert, 1978). Cell extracts for electrophoresis were prepared by five consecutive freezing and showing cycles (liquid nitrogen) of single hair follicles in a small plastic centrifuge tube (Evergreen Sci. Co., Catalog No.3014) with 5 μl of 0.5 M Tris-HCl buffer (pH 6.8), then mixing 5 μl of the solution consisting of 20% glycerin, 0.002% Bromphenol blue, and Tris-HCl buffer (pH 6.8), followed by centrifugation at 16,000 g for 10 min at 4°C. Cell extract from 5 μl to 10 μl was usually applied. In the case of β-hexosaminidase, after electrophoresis the gel was covered with 1% of agar gel solution containing 4-methyl umbelliferyl-N-acetyl β-D-glucosaminide (0.1 mg/ml), in 0.1 M disodium phosphate-citric acid buffer (pH 4.5). The β-hexosaminidase activities were observed by exposing the gel to a long wave ultraviolet light (365 nm). Two major forms of β-hexosaminidase, isozymes Hex A and B were expressed in the outer root sheath and bulb of single hair follicles. The zymograms showed a similarity between the Hex A and

Hex B of the outer root sheath and bulb from hair follicles. However, mobilities of the isozymes in the serum showed a marked difference from those of hair follicles. These findings suggest that the difference between the serum and the tissues and cells is caused by epigenetic modification.

89. Studies on Hereditary Hemolytic Anemia due to Red Cell Adenosine Deaminase Overproduction—Purification and Properties: Hisaichi FUJII, Shiro MIWA (3rd Dept. Int. Med., Yamaguchi Univ., Ube), **Koichi SUZUKI** (2nd Dept. Biochem., Tokyo Univ., Tokyo) **and Hiroyuki ASANO** (Urawa City Hosp., Urawa)

Recently we discovered a case of red cell adenosine deaminase (ADA) overproduction associated with hereditary hemolytic anemia. The patient was a 38 years old male who had hemoglobin, 15.8 g/100 ml; reticulocyte count, 4.5%; serum indirect bilirubin, 4.9 mg/100 ml; ^{51}Cr-labeled red cell half-life, 12 days. The red cell ADA activity was markedly increased (40-fold). The concentration of ATP was 49% of normal controls. The normal red cell ADA was purified 234,000-fold using antibody affinity chromatography with a yield of 23.5%. The specific activity of 94.0 U/mg protein was obtained. The patient enzyme was also purified by the same methods. The specific activity of the patient enzyme was 98.5 U/mg protein. The preparations obtained were homogeneous judging from sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Both enzymes were very similar, there being no significant difference between them in molecular weight (44,000), polyacrylamide gel electrophoresis (common ADA 1-1 phenotype), Michaelis constant for the substrate, thermal stability, optimum pH (7.3), immunological reactivity, and amino acid composition. From this physicochemical and kinetic properties of the patient enzyme in comparison to the normal enzyme, the greatly increased red cell ADA activity seems to be an overproduction of normal enzyme and might be due to the failure of the genetic control mechanism such as marked increase in activity of δ-aminolevulinic acid synthetase in intermittent acute porphyria. It is already accepted that the catalytic activity of the various tissue isozyme of the ADA enzyme resides in a single molecule coded at the same genetic locus. But the lymphocyte ADA of this case was normal. The precise cause of the overproduction restricted in erythroid precursors remains to be proven.

90. High Resolution Two-Dimensional Gel Electrophoresis of Serum Proteins: Tomotaka SHINODA, Kiyotsugu KOJIMA, Kei MANABE and Tetsuo OKUYAMA (Dept. Chem., Tokyo Metropol. Univ., Tokyo)

The two-dimensional gel electrophoresis was applied to the analysis of human serum proteins and red cell enzymes, and more than 200 different spots have been resolved in the

pattern produced in the case of serum proteins. The technique adopted the isoelectric focusing in the first dimension, using a 4% gel (5×140 mm) column of pH gradient from 3.5 to 10, and the electrophoresis was done at 460 V for 20 hr, at 0–4°C. After the run the gel was taken off the column, and placed on a 2nd dimensional gel slab of 4×140×140 mm in size which was prepared in a linear gradient (4 to 21% in the analysis of proteins of molecular weight 40,000 and over, or 4 to 30% for those of 8,000 to 60,000) in Tris-glycine buffer. The electrophoresis continued at 36 mA for 20 hr at 4°C. After the run in the 2nd dimension, the gel was stained with 0.025% Coomassie Briliant Blue to detect proteins, and histochemical methods to detect enzymes. On the routine analysis, 50 μl of serum was used, and 200–210 independent protein spots could be detected on the gel. Among these 24 have so far been identified: these are prealbumin, albumin, α_1-acid glycoprotein, α_1-antitrypsin, thyroxine-binding protein, GC-globulin, ceruloplasmin, retinol-binding protein, α_2-HS-glycoprotein, haptoglobin 1-1, 1-2, 2-2, α_2-macroglobulin, cholinesterase, hemohexin, transferrin and its variants, cold insoluble globulin, β_2-glycoprotein I, immunoglobulins A, G, M, D, E lipoproteins of different sizes, fibrinogen, plasminogen and C3 and other compliments. Since the technique employed neither detergents such as SDS, a most frequently adopted one in the other methods, nor denaturation agents, proteins and enzymes existed in the native state, which enabled the use of varying detection techniques including the histochemical and immunochemical procedures. Genetic variants involving charge (isoelectric point) or molecular weight differences can be routinely detectable in at least 24 proteins at once, facilitating studies of genetic variations in man.

91. The Distribution of Polymorphic Traits in Korea: Koji OHKURA, Tsutomu MIYASHITA (Dept. Human Genet., Tokyo Med. Dent. Univ., Yokyo), **Hayato HASEKURA** (Dept. Forensic Med., Saitama Med. Coll., Saitama), **Yun Sun KANG and Chung Choo LEE** (Dept. Zool., Seoul Nat. Univ., Seoul)

Since 1973, we have analyzed several traits to compare the genetic structure of Korean populations. So far, 12,378 blood specimens were obtained from nine populations (Kwangha-Do, Seoul, Wonju, Chonju, Taegu, Kyungsan, Kwangju, Pusan and Cheju) in Korea. In addition, we obtained 624 blood specimens from Kyungsan for analysis of several traits, and for screening test of acatalasemia 633 specimens from Chungju and 709 specimens from Taejun. One case of hypocatalasemia was screened from 624 specimens and totally we screened only one case of hypocatalasemia from 2,268 specimens in Kyungsan. One case of hypocatalasemia was screened from both Chungju and Taejun. Up to present day, 27 hypocatalasemics were found in 12,378 Koreans and then the gene frequency of acatalasemia was estimated as 0.0011. This value is almost the same as Japanese. The following results were obtained in blood groups from 232 specimens in Kyungsan. ABO:

p=0.296, q=0.209, r=0.495. MNSs: MS=0.0467, Ms=0.4964, NS=0.0460, Ns=0.4109. Rh pheno: R_1R_1=98, R_1R_2=100, R_2R_2=22, R_1r=12. Diego: Di^a=0.0758, Di^b=0.9242. Duffy: Fy^a=0.9375, Fy^b=0.0625. Kidd: Jk^a=0.4504, Jk^b=0.5496 and P: P+=44.83%. The gene frequency of Hp^1 was estimated as 0.275 among 231 specimens, Gc^1 0.722 among 115 specimens and PGM_1^1 0.760 among 231 specimens. The genetic distances from Kyungsan to Seoul, Wonju, Chonju, Kwangju, Pusan and Cheju were estimated as 0.0427, 0.0646, 0.0250, 0.0533, 0.0577 and 0.0516, respectively. For the estimation, the root method was applied for the traits, blood groups (ABO, MN, Rh), haptoglobin, Gc, PGM and acatalasemia.

92. The Distribution of α_1-Antitrypsin Phenotypes in Japanese Detected by Slab Gel Isoelectric Focusing: Kazuhiko MIYAKE, Hiroshi SUZUKI, Hiroshi OKA, Toshitsugu ODA (First Dept. Int. Med., Tokyo Univ., Tokyo), **and Shoji HARADA** (Dept. Leg. Med., Tsukuba Univ., Ibaraki)

α_1-Antitrypsin (α_1-AT) is a polymorphic protein in the serum which inhibits a variety of proteases. There are more than 25 variants reported. A new method of isoelectric focusing (IEF) for α_1-AT phenotyping has been developed to demonstrate advantages over the traditional acid starch gel electrophoresis (ASGE). By means of this technique common MM can further be classified into three subtypes, namely M_1M_1, M_1M_2, M_2M_2. We report here the phenotype distribution of Pi subtypes in Japanese. Materials and Method: Sera from 1,271 healthy adult Japanese were examined. 6.8% polyacrylamide gel contained 3.6% Ampholine (LKB, pH 4–6). IEF was carried out under cooling system for 6 hr with increasing voltage (300→1,000 V). Protein staining was done by Coomassie Brilliant Blue. Results and Discussion: Results obtained from 1,271 are as follows: M_1M_1 886 (69.7%), M_1M_2 316 (24.9%), M_2M_2 62 (4.9%); rare variants 7 (0.6%) —E_{Tokyo} M_1 2, IM_1 1, M_1N 2, M_1S 1, M_2P 1. In Japanese the frequency of rare variants is quite low (0.6%) compared to that in European countries where 5–10% rare variants are reported. No Z variants with the deficient level of α_1-AT in serum were found. New fast variant, heterozygote of E_{Tokyo} was detected, which migrated faster than reference E kindly provided by Dr. M.K. Fagerhol. It behaved similar to E on ASGE. Two cases of E_{Tokyo} M_1 were confirmed inherited by family studies. The frequencies of the common M subtypes (Pi^{M1}=0.83, Pi^{M2}=0.17) are close to those reported for Caucasians. However, the subtype distribution was not found to be in good Hardy-Weinberg equilibrium. This is due to an excess of homozygotes of M_2. There might be the possibility of further microheterogeneity in the M subtypes.

93. Studies on the Incidence of G6PD Deficiency in Japan Using Both Beutler's Spot Test and Starch Gel Electrophoresis: Tadako NAKATSUJI and Shiro MIWA (The Third Dept. Int. Med., Yamaguchi Univ., Ube)

The exact incidence of glucose-6-phosphate dehydrogenase (G6PD) deficiency in Japanese population has been unclear. To study this, G6PD spot test by Beutler and starch gel electrophoresis in phosphate buffer (pH 7.0), Tris-EDTA-borate buffer (pH 8.5) and Tris-HCl (pH 8.8) were performed. Two thousand and six hundred blood specimens from male patients seen at the Yamaguchi University Hospital were used for this study. Thirteen out of 2,600 blood specimens (0.5%) were revealed as erythrocyte G6PD deficiency. Characterization of the enzyme was carried out according to the standard methods recommended by the WHO Scientific Group. The 13 G6PD-deficient cases could be divided into following five groups. Group 1 was comprised of 6 subjects with a electrophoretic mobility between 105% and 114% as compared to the normal B. This variant was named G6PD Konan. Group 2 was comprised of 4 subjects, which were similar to G6PD Konan, but were differentiated from the latter by increased Ki [NADPH]. This variant was consistent with G6PD Ube, which we reported previously. Group 3 was comprised of 1 subject with only low erythrocyte G6PD activity, 37% of normal B. This variant was consistent with G6PD B(−) Chinese. Group 4 was comprised of 1 subject with a little faster electrophoretic mobility, 64% of normal B. This variant was designated G6PD Kiwa. Group 5 was comprised of 1 subject. This variant was similar to G6PD Kiwa except for normal electrophoretic mobility. This variant was named G6PD Kamiube. All of these 5 groups showed normal Km G6P, Km NADP, 2dG6P and dNADP utilization rates, thermostability and pH optimum curves. Family studies with Konan, Ube and B(−)Chinese variants confirmed X-linked inheritance. We are not sure whether G6PD Konan and Ube, which have higher incidence than other variants, are distributed all over Japan, or not. But at least in Yamaguchi prefecture, the incidence of G6PD deficiency is not so low as that described before.

94. Rare Electrophoretic Variants Found in Hiroshima and Nagasaki Residents: Jun-ichi ASAKAWA, Mikio FUJITA, Kazuaki GORIKI, Takeshi KAGEOKA, Shotaro NERIISHI, Sadahisa KAWAMOTO, Howard B. HAMILTON, Chiyoko SATOH (RERF, Hiroshima and Nagasaki) **and Naoki UEDA** (Kochi Pref. Hosp., Kochi)

A study on protein variants was conducted on about 2,800 residents of Hiroshima and Nagasaki during the period from 1972 to the end of June, 1978, using thin layer starch gel electrophoresis based on a total of 26 different proteins, *i.e.*, 4 types of serum protein, hemoglobin A and A_2 and 20 types of erythrocyte enzymes. Of these proteins, 6 types

in whom polymorphs are known, *i.e.*, Hp, AcP, ADA, PGM_1, 6PGD and Esd, had gene frequencies which were within the range reported for other Japanese population. Introduced in this report are several rare variants of interest encountered during the course of our study. Three cases of PGM_2 variants were noted, two of which showed a pattern similar to PGM_2 1-9 reported by Blake and Omoto,[1] while the other resembled PGM_2 1-5 reported by Parrington *et al.*[2] One individual from Nagasaki showed a slow migrating set of isozymes of TPI together with a normal set of the isozymes. The pattern of a CA II variant showed normal band with one migrating cathodally. Three cases of NP 1-2 were also noted. All of these except one case of NP 1-2 were confirmed to be genetic variants based on results of family studies.

1) Blake, N.M. and Omoto, K. 1975. Phosphoglucomutase types in the Asian-Pacific area: a critical review including new phenotypes. *Ann. Hum. Genet., Lond,* **38**: 251-273.
2) Parrington, J.M., *et al.* 1968. Linkage relationships between the three phosphoglucomutase loci PGM_1, PGM_2 and PGM_3. *Ann. Hum. Genet., Lond.,* **32**: 27-34.

95. Human Red Cell GPT Polymorphism: Comparison of the Activities Using Pyruvate and L-Glutamate as Substrates: Shintaroh UEDA, Keiichi OMOTO (Dept. Anthrop., Univ. Tokyo, Tokyo) **and Makoto UCHIKAWA** (Blood Transfusion Service, Tokyo Univ. Hosp., Tokyo)

Genetic polymorphism of soluble Glutamic-pyruvic transaminase (s-GPT) was demonstrated in human red blood cells (Chen and Giblett, 1971) and the differences in the average activity between the three common phenotypes have been reported. Namely, the mean activity of GPT 1 is about 1.5 to 3.5 times higher than that of GPT 2, and that of GPT 2-1 is nearly intermediate. These reports, however, have thus far been limited to the reaction using L-alanine and α-ketoglutarate as substrates although this enzyme catalyzes the reversible reaction. In the present study, we report the results of measurements of red cell GPT activity using pyruvate and L-glutamate as substrates. Red cell GPT activity was determined by measuring the amount of α-ketoglutarate formed in the reaction, using a selective microphotometric method. The measurement of α-ketoglutarate was carried out on the basis of a colour reaction with diazotized sulfamethizole in a sodium hydoxide solution in the presence of sodium sulfite and sodium hypophosphite (Hamada and Ohkura, 1976), with slight modifications. The assay of red cell GPT enzyme activity was performed on fresh haemolysates obtained from 164 blood donors in Tokyo. The mean activities of the three common phenotypes were found to be 0.356 [units/gHb] for GPT 1, 0.281 [units/gHb] for GPT 2-1, and 0.259 [units/gHb] for GPT 2, with standard deviations 0.106, 0.086, and 0.086, respectively. The difference in the mean activities between GPT 1 and GPT 2 was statistically significant ($t=4.473$, $p<0.005$). Thus, it was

found in the both reactions that the mean activity of GPT 1 is higher than that of GPT 2 and that of GPT 2-1 falls between these two levels.

96. Genetic Polymorphisms and Some Properties with Respect to Phenotypes of Human Red Cell Glutamic-Pyruvic Transaminase: Itsuro NISHIGAKI, Tohru ITOH, Haruo SUZUKI and Norio FUJIKI (Dept. Epid. & Genet., Inst. Develop. Res., Kasugai)

Since it was shown by Chen and Giblett (1971) that human red cell GPT exhibited a genetic polymorphism, many authors have reported data on the distribution of two common alleles, Gpt^1 and Gpt^2, from various ethnic populations. In addition, quantitative differences in enzyme activity among the three common phenotypes of GPT 1, GPT 2-1 and GPT 2 have been also demonstrated by several authors. In the present study, we report comparative data on the distribution of the GPT allele frequency among three different populations in Japan, one of which is urban, while the other two are isolated, and also on the differences of the GPT activity with respect to phenotypes among 376 individuals selected from these samples. The Gpt^1 frequencies of 0.663 and 0.528 derived from the two isolates revealed somewhat different values, lying outside those for other Japanese populations, due to probably highly inbred structure and small sample size. In enzyme assay, the GPT activity among three common phenotypes showed gene dosis relationship and mean values were found to be 6.47 units/gHb for GPT 1, 4.52 for GPT 2-1 and 2.65 for GPT 2. The result suggested that as an average, the Gpt^1 product in the red cell has catalytic activity about 2.5 times higher than that of Gpt^2. Of these samples, two cases were clarified to be heterozygotes for the silent allele through the methods of electrophoretic determination, quantitative enzyme assay and concomitant pedigree study. Furthermore, the two types homozygous of GPT 1 and GPT 2 were partially purified from human erythrocytes and their biochemical characteristics compared, in order to clarify their properties. In the determination of substrate affinity, apparent Michaelis constants for GPT 1 and GPT 2 were estimated to be 0.85 mM and 0.70 mM for the Km α-KG and also 20.0 mM and 16.7 mM for the Km alanine, respectively. The results for thermostability over the range of temperatures 45–60°C and for pH optima between 6.5–9.0 appear to show a certain significant difference between two isoenzymes of GPT 1 and GPT 2. The GPT 1 enzyme has been relatively more stable than the GPT 2 under the conditions of temperatures more than 55°C and pH values less than 6.5. Henceforth, further biochemical and genetic studies will be necessary in order to explain the quantitative differences between the red cell GPT activity of the three common phenotypes.

97. Study on Genetic Polymorphisms in Isolated Community (VIII)—Tomiyama Village: **Itsuro NISHIGAKI, Tohru ITOH, Norio FUJIKI** (Dept. Epid. & Genet., Inst. Develop. Res., Kasugai) **and Keiichi OGURA** (Tohei Hosp., Aichi)

We have continuously investigated the genetic constitution and blood polymorphisms in several isolated communities in Western Japan. In the present study, we report the data obtained by the field survey in Tomiyama village, Aichi Prefecture, where the bleeding structure has been completely clarified through Koseki record checking. Among 243 inhabitants in 79 households in Tomiyama we have checked 216 inhabitants in the course of medical survey and collected 188 blood samples for the past three years. There revealed first cousin marriage rate of 11.6%, consanguinity rate of 31.9% and mean inbreeding coefficient of 0.01213, that is, all villagers have had almost same coefficient with second cousin marriages. In this community, the allele frequencies of various genetic polymorphic traits, such as I^A=0.224, I^B=0.227, G^N=0.414, Hp^1=0.170, Tf^D=0.093, p^a=0.235, ADA^2=0.014, EsD^2=0.362, Gpt^2=0.333, PGD^c=0.114, $PGM_1{}^2$=0.261 and $PGM_1{}^7$=0.035 were calculated. These values were slightly different from those of neighbouring populations, due to probably genetic drift and highly inbred small sample size. On the PGM distribution, a high frequency of the $PGM_1{}^7$ allele (=0.035) was revealed and one rare individual homozygous for this allele was detected among those in the community. A comparative investigation of relative PGM_1 activity among six phenotypes observed ($PGM_1$1, $PGM_1$2, $PGM_1$7, $PGM_1$2-1, $PGM_1$7-1 and $PGM_1$7-2) was performed to clarify enzyme characteristics for the $PGM_1{}^1$, $PGM_1{}^2$ and $PGM_1{}^7$ allele products. Total PGM activity was measured by a modified version of the method described by Beutler *et al.* (1977) and the mean value in the red cell has presented 2.01±0.32 IU/gHb among 64 individuals examined. A densitometric assay was carried out to determine the relative activity ratio of the PGM_1 and PGM_2 isoenzymes. The relative PGM_1 activity for the homotypes is as follows: 0.72±0.12 IU/gHb for $PGM_1$1, 0.81±0.22 for $PGM_1$2 and 0.78 for $PGM_1$7. From these results, enzyme activity of the $PGM_1{}^2$ allele product appears to be slightly higher than that of $PGM_1{}^1$. However, mean values for the heterotypes are found to be lower than presumable values from those for the homotypes in relative PGM_1 activity measurements and even in total enzyme assays. Henceforth, further studies on much more blood samples will be necessary to determine conclusive results.

98. Frequencies of Genetic Markers in Saliva in Japanese: **Shigenori IKEMOTO** (Dept. Legal Med., Jichi Med. Sch., Tochigi) **and Kiyoshi MINAGUCHI** (Dept. Forensic Odont., Tokyo Dental Coll., Tokyo)

Salivary genetic marker systems provide much information in human genetics and their application to legal medicine. In 1976, we have reported the gene frequencies of six sali-

vary genetic marker systems in Japanese, Pa, Pb, Pr, Db, Pm and Amy_1. We are reporting results obtained from further examination of these systems and, in addition, of another new system, Ph. There were no significant differences between the present and previous reports. The gene frequencies obtained were 0.211 for Pa^+, 0.789 for Pa^-, 1.00 for Pb^1, 0 for Pb^2, 0.765 for Pr^1, 0.235 for Pr^2, 0.056 for Db^+, 0.944 for Db^-, 0.012 for $Amy_1{}^v$, 0.988 for $Amy_1{}^n$, 0.401 for Pm^+, 0.599 for Pm^-, 0.026 for Ph^+ and 0.974 for Ph^-. The frequencies in Pa, Pb, Pr, Db and Amy_1 systems in Japanese were compared with other racial groups. The gene frequency of Pb^+ in Japanese (0.056) was lower than Caucasians (0.12), Negroes (0.56) and Chinese (0.07), while the frequency of Pb^1 in Japanese (1.000) was higher than Caucasians (0.995) and Blacks (0.84). Frequencies of Pr^1 (0.765) and $Amy_1{}^v$ (0.012) in Japanese were somewhat higher than those of Caucasians, 0.73 and 0.005, but lower than Blacks, 0.80 and 0.039, respectively. Frequency of Pa^+ (0.214) in Japanese was almost the same as that in Caucasians (0.214) but higher than Blacks (0.14). Comparison was not carried out in the Pm and Ph systems.

99. Regional Mapping of Human Chromosome 13: Assignment of the Gene for Esterase D to 13q21→q22: Hidetsune OISHI, Itsuro NISHIGAKI (Dept. Genet. & Epid., Inst. Develop. Res., Aichi Pref. Colony, Kasugai), **Tsutomu YAMANAKA and Katsuya TSUDA** (Cent. Hosp., Aichi Pref. Colony, Kasugai)

Van Heyningen *et al.* (1975) suggested that human esterase D (ESD) was coded for by a gene on chromosome 13 from concordant segregation analyses of enzymes and chromosomes in man-mouse somatic cell hybrids. In addition, Robson *et al.* (1976) reported that the structural gene for ESD lay in 13q2 or q3 by linkage analyses in families including ones with abnormalities of chromosome 13. In the present study, we report a boy with 13q-syndrome, whose chromosomes were investigated by the trypsin and fluorescent banding techniques. Isozyme patterns of esterase D in the red cell of the patient and his parents were also examined. The patient was born August 22, 1975, after 40 weeks of gestation, as the second child of a 29 year-old mother and a 33 year-old father, The parents were not consanguineous. At birth, the boy weighed 2,240 g and was found to have multiple abnormalities; mental retardation, microcephaly, hypertelorism, broad nasal bridge, malformed ears, high-arched palate, micrognathia, short neck, retentio testis (left), small penis, dislocation of the hips, transverse palmar creases, single flexion creases on the 5th finger, fusion of the 4th and 5th metacarpals and hypoplastic thumbs, but no retinoblastoma. Chromosomal analyses of the patient revealed that one of the chromosomes of group D was deleted. By the differential staining with trypsin-Giemsa (G) and BudR-acridine orange (R) methods, a distal half of the long arm of chromosome No. 13 was missing. However, no evidence of translocation of the deleted material onto other chromosomes

was noted. Therefore, the karyotype of the patient could be written as 46,XY,del(13)(q22). His parents had apparently normal chromosome sets. After starch-gel electrophoresis, isozymes of the red cell esterase D were detected with the use of 4-methyl umbelliferyl acetate as substrate. The isozyme patterns of the patient, his mother and father were ESD 2-1, ESD 2 and ESD 1, respectively. These results showed that the structural gene for ESD was still remained in the cells of patient. Therefore, it is concluded that the gene for ESD lie in 13q21 or q22, that is, in 13q2.

100. Gene Dosage Study on Chromosomal Aberration Syndrome. (3) The Erythrocytic Enzyme Activities for the Patient with Aberrant Chromosome 2: Hiroshi NAKAI, Michiko ADACHI, Hiromi OTOMO, Norihiro ARAI, Shigeo HISA and Keiya TADA (Dept. Pediat., Tohoku Univ., Sendai)

Gene dosage studies were performed on the erythrocytic enzymes of the patient with 47,XY,del(2)(p21),+r. The gene locus of acid phosphatase-1 (ACP-1) is on the short arm (p23) of chromosome 2 according to the recent gene mapping. Proportional decrease or enhancement of the enzyme activity in patients with monosomy or trisomy of the short arm of chromosome 2 were reported by Gerguson-Smith *et al.* (1973) and Magenis *et al.* (1975). The aberrant chromosome, del(2)(p21), of our case should not contain the ACP-1 gene locus. Therefore, a normal activity and an electrophoretic pattern of the enzyme observed in the patient suggested the existence of the ACP-1 gene locus on the extra ring chromosome. As there was no remarkable discrepancy in the clinical features and banding pattern, the extra ring chromosome is considered to have been derived from chromosome 2. On the other hand, it was suggested that the galactose-1-phosphate uridyl transferase (GALT) gene is located on the chromosome 2 by Chu *et al.* (1974), while on the chromosome 3 by Tedesco *et al.* (1974) and on the chromosome 9 by others. If the extra ring chromosome of the patient had been derived from the chromosome 2, the patient should be trisomic for the proximal portion of the chromosome as well as for the provisional gene locus of GALT enzyme (p13-q12), and the enzyme activity might be enhanced to 1.5 times of normal controls. But the real activity of the enzyme was in normal ranges. Therefore, the gene locus is located probably not on the chromosome 2, at least, on its proximal portion.

101. Gene Dosage Effect of LDH-B Gene in the Red Cells and Fibroblasts Drived from the Patients with 12p Trisomy Mosaicism: Ikuko KONDO and Hideo HAMAGUCHI (Dept. Human Genet., Tsukuba Univ., Ibaraki)

On the basis of linkage studies and man-mouse or man-hamster hybrids experiments, the gene of human triosephosphate isomerase (TPI), glyceraldehyde 3-phosphate de-

hydrogenese (GA3PD) and lactate dehydrogenase-B (LDH-B) have been assigned to the short arm of chromosome 12, and enolase-2 (ENO-2) was also assigned to the portion between 12q12 and 12pter. In order to examine the gene dosage effects of these loci, total activities of TPI, GA3PD, LDH, ENO together with other enzymes of the glycolysis pathway in the red cells derived from a 13-year-old male patient whose karyotype was 46,XY (34%)/47,XY,+12p(67%) in both peripheral lymphocytes and cultured skin fibroblasts, were examined. Furthermore, electrophoretic analyses of LDH were examined in the red cells and fibroblasts. LDH and GA3PD activities of red cells were significantly increases and these values corresponded to 151 and 136 percent of the average values of normal controls, respectively. Although TPI and ENO activities corresponded to 144 and 135 percent of the average values of controls, the activities were within normal ranges. The ratio of the LDH-B products to LDH-A products was analysed by densitometric analysis after agar gel electrophoresis of extracts from red cells and cultured skin fibroblasts. In both red cells and fibroblasts, the ratio of LDH-B products and LDH-A products was about 1.3 times as much as the ratio of normal controls. These data suggest that gene dosage effects are present in LDH-B locus and GA3PD locus, and possibly in TPI locus and ENO locus.

102. Growth Characteristics and Biochemical Properties of Cultured Skin Fibroblasts Derived from Patients with Familial Polyposis Coli: Hideo HAMAGUCHI, Fumitaka MORITO and Ikuko KONDO (Dept. Human Genet., Tsukuba Univ., Ibaraki)

It has been reported that cultured skin fibroblasts derived from patients with familial polyposis coli show abnormal growth characteristics, most of which are partly similar to those of transformed cells. In order to characterize the growth characteristics and biochemical properties of the cultured skin fibroblasts derived from patients with familial polyposis coli, we examined various items of cultured fibroblasts derived from patients with polyposis and compared with those of cultured skin fibroblasts derived from healthy controls who are not related to the patient with polyposis, those of an adult fibroblast transformed by SV 40 virus (W98-Va-C), and those of a fetus fibroblasts (IMR 90). The items examined include serum requirements, contact inhibition, colony-formation rates, clonal morphology, Ca^{2+} requirements, cystine requirements, fatty acid composition, LDH isozyme patterns, amounts of large external transformation-sensitive (LETS) protein, and amounts of a cytoplasmic protein which is found to be increased in transformed fibroblasts by us. There were no differences in all items examined between cells from patients and cells from controls, though consistent differences were observed in all items between cells from patients or from controls and the transformed cell or the fetus cell. These data suggest that

the growth characteristics and biochemical properties of cultured skin fibroblasts derived from patients with familial polyposis coli are fundamentally very similar to those of cultured skin fibroblasts derived from healthy controls.

103. Relation of DNA Repair Activity Due to UV Induced Damage between Cockayne's Syndrome and Xeroderma Pigmentosum: Hiroshi TANAKA, Junichiro FUJIMOTO, Toshie ITO and Tadao ORII (Dept. Pediat., Gifu Univ., Gifu)

Cockayne's syndrome is a rare hereditary disease inherited as an autosomal recessive trait. Characteristics of this disease are typical appearances (microcephalus, large ears, large nose and sunken eyes), severe dwarfism, mental retardation, dermal photosensitivity, retinitis pigmentosa and deafness. Malignancy of the syndrome in older age was reported in one case by Robbins *et al.* The congenital abnormalities of this syndrome and carcinogenesis may be interacted in repair mechanism affected by UV and carcinogens as in the Xeroderma Pigmentosum (XP). We have investigated the UV sensitivities and DNA repair mechanism induced by UV and carcinogens (4NQO, MNNG) in two siblings of Cockayne's syndrome (6 1/2 year-old boy and 1 1/2 year-old boy). Cells from these two brothers had high sensitivities to UV and 4NQO, being severely decreased in ^{3}H TdR incorporation resembling to XP cells, in which UV induced unscheduled DNA synthesis was less than 4% of control cells. These results show that DNA repair activity of Cockayne's syndrome due to UV induced damage was similar to that of XP.

104. Thermostability of Glucose Phosphate Isomerase Isozymes: Chiyoko SATOH (RERF, Hiroshima) **and Harvey W. MOHRENWEISER** (Dept. Human Genet., Univ. Michigan, Ann Arbor, Michi.)

Gel electrophoresis is widely used in screening for protein variants. However, proteins in which the electric charge of the whole molecule differs from normal are detectable by this method. Further, hidden among variants considered to be electrophoretically identical, are proteins with different amino acid substitutions. Even among proteins which do not differ electrophoretically, if a substituted amino acid is different, it is likely that the conformation of the molecule will be changed, possibly resulting in change in its stability or reactivity. The thermostability of the five kinds of electrophoretically variant phenotypes of GPI which were found in Japanese in a previous study (Tanis *et al.*, 1978) was examined. The most frequently found variant phenotype, termed GPI 1-$4_{HIR\,1}$ could be divided into distinct three classes on the basis of thermostability characteristics. Hemolysates from 20 individuals with the GPI 1-$4_{HIR\,1}$ phenotype were heated to 47°C, 49.5°C and 52.5°C for 15 and 30 min after which the residual GPI activity was compared with that of the normal type (GPI 1) subjected to the same conditions. Two of the variant

enzymes were very labile, 16 were more stable than these 2, but less stable than the normal type and the other 2 cases showed almost the same thermostability as that of the normal. Starch gel electrophoresis was conducted on the hemolysates after heating and it was observed that thermostability was a characteristic of the variant protein molecule but not of the electrophoretically normal molecule. The order of the stability of these 3 kinds of variants against 5 M urea was the same as that of their thermostability. No difference against inhibition by 6-phosphogluconate was observed among the normal and the variant glucose phosphate isomerases. Family studies confirmed the genetic nature of the thermo- and urea stability differences among the affected individuals.

Tanis, R.J., Ueda, N., Satoh, C., Ferrell, R.E., Kishimoto, S., Neel, J.V., Hamilton, H.B., and Ohno, N., 1978. The frequency in Japanese of genetic variants of 22 proteins IV. *Ann. Hum. Genet., Lond.*, **41**: 419.

105. Genetic Polymorphism of the Fourth Component of Human Complement in Japanese: Katsushi TOKUNAGA, Satoshi HORAI, Keiichi OMOTO (Dept. Anthrop., Tokyo Univ., Tokyo), **Takeo JUJI** (Blood Transfusion Service, Tokyo Univ. Hosp., Tokyo) **and Hachiro NAKAJIMA** (Dept. Forens. Med., Tokyo Med. Dent. Univ., Tokyo)

Polymorphism of the fourth component of human complement (C4) was investigated in Japanese using an agarose gel electrophoresis and a slab polyacrylamide gel electrophoresis followed by immunofixation. Monospecific anti-human C4 antiserum was produced by immunizing rabbits with C4 purified from fresh plasma by sodium sulphate precipitation, DEAE cellulose chromatography, Sephadex G-200 gel filtration and preparative disc electrophoresis. Samples used for C4 typing were either heparinized plasma or the ACD-plasma to which at least 10 mM EDTA in the final concentration was added. Serum was not suitable for electrophoretic separation because of the alteration of mobility due to conversion of C4. In one method, electrophoresis was carried out at 15 V/cm (4°C) for 3 hr in the 1.2% agarose gels with a continuous 0.1 M Tris–0.04 M glycine buffer (pH 9.0). In the other method, a thin layer vertical slab polyacrylamide gel electrophoresis was carried out using the disc electrophoresis system of Ornstein and Davis with the exception, that the concentration of the separation gel was 4%, instead of the original 7.5%. Immunofixation was performed by overlaying antiserum on the gel surface after the electrophoresis for 1–1.5 hr at room temperature. The gel was then washed for 24 hr (agarose) to 48 hr (polyacrylamide) in saline and stained with Coomassie Brilliant Blue. Three phenotypes were observed: one mainly with the fast migrating bands (F), one mainly with the slow migrating bands (S) and the one with both bands (FS). Typing of the family material consisting of 47 parents and 93 offsprings showed no discrepancy from the postulate that the C4 polymorphism is controlled by a pair of codominant alleles, $C4^F$ and

$C4^S$. The samples of unrelated, healthy adults were examined. In a sample (N=103) from Kamogawa City, Chiba Prefecture, which was mainly typed by agarose gel immunofixation electrophoresis, allele frequencies for $C4^F$ and $C4^S$ were estimated to be 0.549 and 0.451 respectively (χ^2=0.633, ldf, 0.50>p>0.30) In the Tokyo sample (N=188), which was mainly typed by polyacrylamide gel electrophoresis followed by immunofixation, the allele frequencies were 0.535 and 0.465 (χ^2=0.135, ldf, 0.80>p>0.70). The difference in the gene frequencies between the two samples was statistically not significant. Future studies are needed to distinguish further C4 phenotypes, since the resolving power of the two electrophoretic systems used in the present study is still to be improved.

106. The Distribution of Subtypes of Serum Gc-globulin in Japanese and the Neighbouring Populations: Keiichi OMOTO (Dept. Anthrop., Univ. Tokyo, Tokyo) **and Kazuhiko MIYAKE** (First Dept. Int. Med., Univ. Tokyo, Tokyo)

Using the thin-layer slab polyacrylamide gel isoelectrofocusing (pH 4–6) followed by "immuno-printing" on cellulose acetate membrane, human serum Gc-globulin, now known as a vitamin D binding protein, is shown to have multiallelic polymorphism. At least four common alleles occur in Japanese, and the average heterozygosity at Gc locus is estimated at 0.6496, while it is 0.3509 if conventional electrophoresis is agar or agarose gels is used. Besides the common Gc subtypes (1F, 1S, 1J and 2), at least three less common subtypes were observed in a sample of 310 unrelated, healthy Japanese living in Tokyo. Two of them were Gc 1 variants and the other Gc 2 variant. We propose to call them: Gc $1TK_1$ (1 Tokyo-1), Gc $1TK_2$ (1 Tokyo-2) and Gc 2Y. On the isoelectrofocusing pattern, Gc $1TK_1$ has the most anodal position, $1TK_2$, 1J, 1F and 1S following in this order. The allele frequency in Japanese is estimated as follows: Gc^{1TK_1} 0.0048, Gc^{1TK_2} 0.0016, Gc^{2Y} 0.0016. The another variant, Gc 1N which has been found to be very common among the Philippine Negrito, has the isoelectrofocusing position intermediate between Gc J and Gc TK_2. The single banded Gc 2Y is slightly less anodal to the cathodal band of Gc 1S. Gc subtypes in a sample of 144 Ainu of Hidaka, Hokkaido, were determined. The distribution of subtypes is not much different from that of the Japanese, the allele frequencies being as follows: Gc^{1F}=0.5214, Gc^{1S}=0.2571, Gc^2=0.2214. Also, the subtypes Gc 1J, Gc $1TK_1$ and Gc 2Y occur among the Ainu. It is interesting, that the last mentioned variant may be more common in the Ainu than in the Tokyo Japanese, although there is uncertainty as to its accurate frequency because the phenotypes Gc 2Y-1S and Gc 2Y-1F may have not been clearly distinguished from Gc 1-1 subtypes. Tentative study of Gc-subtyping of a Philippine Negrito population indicates that, similar to the Japanese and the Ainu data, Gc^{1F} has a higher frequency (0.457) than that of Gc^{1S} (0.181). Therefore, the ratio Gc^{1F}/Gc^{1S} among the population groups in the Far East thus far examined forms

striking contrast to that obtained for European and Amerindian populations thus far reported by Constans and his colleagues, in which a much higher Gc^{1S} frequency than Gc^{1F} was observed.

107. 日本人に見出される Gc 変異型：石本剛一・鍬田美江子（三重大・法医），**中嶋八良**（東医歯大・法医）. **Gc Variants in Japanese:** Goichi ISHIMOTO, Mieko KUWATA (Dept. Legal Med., Mie Univ., Tsu) and Hachiro NAKAJIMA (Dept. Forens. Med., Tokyo Med. Dent. Univ., Tokyo)

以前，免疫電気泳動を用い日本人の Gc 型を再調査し，Gc 1-1, 2-1, 2-2 以外に集団の5％程度に Gc J-1, J-2, J-J の存在することを知ったが，この際 Gc J-1 の判定に苦しんだので，等電点電気泳動を用いる Gc 変異型の分析を試みた．試料は Gc J 既知血清55例，集団調査のため集めた三重および東京の学生，献血者820例である．等電点電気泳動で Gc J 既知血清を調べると2種類の異なる変異型，すなわち Gc 1F より若干陽極側に出現する2成分 (Gc J) と Gc 1fast をはさんでより陽極側に出現する2成分 (Gc JF) があり，それらが Gc 1F, 1S, 2 と組み合わされた表現型および J-J, JF-JF が検出された．さらに J, JF を再検査すると，Gc J の少数はわずかに等電点の低い2成分 ($Gc\ J_2$), JF の1例は若干高い等電点をもつ成分 ($Gc\ JF_2$) に区別された．さらに集団調査から Gc 1 slow をはさむ2成分をもつ2例の変異型 (Gc Mie) および別の1家族には Gc 1S より遅く出現する2成分をもつ変異型 (Gc Okada) があった．Radial immunodiffusion で血清 Gc の定量を試みると，正常型は subtype に関係なくほぼ一致した値を示し（50例平均 49.7 mg/100 ml），Gc J のヘテロ接合型は 31～39 mg/100 ml（30例），ホモ接合型は 27.2 mg/100 ml（2例）と低値を示した．Gc JF のヘテロ接合型は正常型の値に類似した（49.6 mg/100 ml, 20例）．等電点電気泳動のパターンが artefact かどうか，1F, 1S, 2, J, JF, Mie 試料について検討した．全血清に vitamin-D_3 添加で段階的に陽極側へシフトするパターンに変化すること，thermolysin 消化ですべての成分は Gc 1F fast より陽極側へ transform すること，neuraminidase 消化で Gc 2 に変化なく他の2バンドからなる Gc はすべて陰極側の1本のバンドに変化することをみた．集団調査で J_2-1F（1例），J_2-1S (2), Mie-1F (2) を除く13表現型の遺伝子頻度は Gc^{1F} 0.473, Gc^{1S} 0.247, Gc^{2} 0.254, Gc^{J} 0.018, Gc^{JF} 0.008 と計算された．

108. A Rare Blood Phenotype Kp(a−b−) Suggesting the Existence of a New Allele, *Kp*^{c}, at the *Kell* Complex Locus: Yasuto OKUBO, Hideo YAMAGUCHI, Taiko SENO, Masayoshi TANAKA (Osaka Red Cross Blood Center, Osaka) **and Kihachiro MATSUSHITA** (Fukuoka Red Cross Blood Center, Fukuoka)

In testing for irregular antibodies the serum of one donor, Mrs. Oka. from the Fukuoka prefecture, was found to contain anti-Kp^{b}. Her cells lacked the Kp^{a} antigen as well as Kp^{b}, though her k, Js^{b} and other Kell antigens were present and normal. Mrs. Oka. 42-year-old was presumably immunized by transfusion in 1965 and perhaps by her two children. The specimen was sent to MRC Blood Group Unit, London, where our serological findings were reconfirmed, and the propositus cells were found to react with the anti-Levay serum.

The Levay is the earliest private antigen recognized in 1946. Thus, it seemed most probable that the propositus is homozygous for a third and new allele Kp^c of the *Kp* part of the *Kell* locus. Pedigree studies showed that her parents were consanguineous (first cousins once removed) and three of the seven sibs were of the same phenotype as the propositus. None of these three Kp(a−b−) sibs has formed anti-Kp^b. Recently three other samples of anti-Kp^c were identified in Osaka donors. Using anti-Kp^a, anti-Kp^b and anti-Kp^c, we tested 1,865 donors' cells selected at random and obtained 6 Kp(a−b+c+) samples (0.32%), the rest being Kp(a−b+c−). The roughly estimated gene frequency of the Kp^c was 0.00162.

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109. On the H Specificity of E Blood Group Antigen: Ken FURUKAWA and Shin YAZAWA (Dept. Legal Med., Gunma Univ., Maebashi)

There are two types of blood group E system. Group E red cells react strongly with anti-H-E eel type II serum and group e red cells react weakly. As the group O red cells react very strongly with the eel serum, they belong to group E. Recently, Yamamoto *et al.* reported that they found the O red cells reacted weakly with eel serum. We found the anti-H-E agglutinin in human serum of group Ae fibrosarcoma patient (F.M.) and also found group Oe person (Y.M.) whose red cells reacted weakly with the eel and the human (F.M.) anti-H-E agglutinins. H specificity of E antigen was investigated by the reaction of OE, Oe (Y.M.), AE and Ae red cells with anti-H-E eel and human (F.M.) sera. Strength of agglutinability of the red cells against the anti-H-E sera was OE>Oe=AE >Ae. When eel and human anti-H-E sera were absorbed with Oe or Ae red cells, anti-A-E agglutinin reacted with OE and AE red cells was unabsorbed. Repeated absorption by Oe or Ae red cells did not change the agglutinin titers of the anti-H-E sera. Anti-H chicken and human Bombay sera and *Ulex europeus* lectin agglutinate OE red cells slightly stronger than Oe red cells. When these sera were absorbed repeatedly with Oe red cells, anti-H agglutinins were completely removed from the sera. The H and H-E antigens were destroyed by the action of α-(1→2)-fucosidase from *Bacillus fulminans*. Then the H and H-E antigenic determinant sugars must be α-(1→2)-fucosyl resdiue linked to β-galactosyl residues. No significant difference of serum α-(1→2)-fucosyltransferase activity of OE and Oe persons was found by the tests of incorporation of [^{14}C]fucose into phenyl-β-D-galactoside in the presence of GDP-[^{14}C]-D-fucose. Transformation experiments of OE and Oe red cells by treatment with group B saliva and UDP-D-galactose resulted very weaker B reactivity with anti-B human serum in tansformed Oe red cells than that of OE red cells. The results revealed that some of α-(1→2)-fucosyl oligosaccharide chains directed to anti-H-E antibodies on the group E red cells and the H-E oligosaccharide may

absent in Oe red cells. It is suggested that the H-E activities of α-(1→2)-fucosyl residues of H-E oligosaccharide chains are almost masked with A antigenic α-(1→3)-*N*-acetyl-D-galactosaminyl residues in Ae red cells and B antigenic α-(1→3)-galactosyl residues in Be red cells.

110. Idiotypic Specificity of Anti-Rh LOR Antibody and Evolution of the Idiotype in 11 Years: Harutaka MUKOYAMA, Shigeru YAMAMOTO (Second Medico-Legal Sec., NIPS, Tokyo), **Jacqueline de SAINT MARTIN and André EYQUEM** (Service d'Immuno-Hémat., IP, Paris)

An anti-idiotypic serum was prepared in three rabbits immunized with Rh (D+C) antibodies isolated from a donor (LOR) serum in 1974. These antisera were absorbed with pooled IgG (Fr II) and $F(ab')^2$ from normal human. The antisera agglutinated at high titers with O R.r red cells coated with the immunizing antibodies and at lower titers with red cells coated with antibodies from LOR serum taken at other years. The anti-LOR idiotypic antiserum was not inhibited by 22 sera of anti-D and 3 sera of anti-D+C(G). The hemagglutination of anti-LOR idiotypic sera by different samples from the same donor (LOR) was completely inhibited with the immunizing serum and partially with other samples. These results show that idiotypes or idiotypic specificities appeared or disappeared during the period studied and present the first observation on evolution of antibody idiotype in human.

111. Determination of Hb A_2 by Means of DEAE Cellulose (DE-52) Column Chromatography: Shunichi SHIMASAKI, Iwao IUCHI, Kazuo HIDAKA (Dept. Biochem., Kawasaki Med. Sch., Kurashiki) **and Satoshi UEDA** (Dept. Int. Med., Kawasaki Med. Sch., Kurashiki)

A method for the determination of Hb A_2 by means of DEAE cellulose (DE-52) microcolumn chromatography (5×0.5 cm) has been improved as a collaboration work with ICSH abnormal hemoglobin groups. The main methodological differences between our method and that of Huisman (*J. Lab. Clin. Med.*, **86**: 700–702, 1975) which might be ready to adopt as a recommendable standard method are as follows: i) To raise up the recovery of Hb A_2 and other remaining Hb component from column; both of Hb collection volume was altered from 4–5 ml to 15.0 ml. This procedure improved much the recovery from usual 80–90% to nearly 100%. ii) To decrease the affinity of Hb with DE-52 and to elute Hb A_2 in a sharp band; the pH of the Developer 1 (Glycine-KCN) and working ion exchangers were adjusted to 7.0, but not originally reported 7.3–7.5. iii) To obtain reliable and consistent Hb A_2 value; an absolute amount of 6–15 mg Hb was needed as an application quantity to the top of the column. This amount corresponds 2 drops of 10 g/dl

Hb solution and not one drop of original method. By these modifications, our method gave quite satisfactory accuracy, namely correlation coefficient (r) between the theoretical and the observed value was $r=+0.999$ in a Hb A_2 range of 1.3–45.6%. The normal adult Hb A_2 value was $3.3\pm0.23\%$ ($n=50$) contrasting 2.5% of the original method. Further studies are, accordingly, necessary before final recommendation of DE-52 micro-column chromatography for Hb A_2 determination.

112. Hb Okayama(α116 Glu→Ala): Its Identity with Hb Ube-4: Kazuo HIDAKA, Iwao IUCHI (Dept. Biochem., Kawasaki Med. Sch., Kurashiki), **Satoshi UEDA, Susumu SHIBATA, Hiroshi HIRANO** (Dept. Int. Med., Kawasaki Med. Sch., Kurashiki) **and Yuzo OHBA** (Dept. Clin. Path., Yamaguchi Univ., Ube)

In 1968, an electrophoretically slow-moving abnormal hemoglobin (Hb Okayama) was discovered in heterozygous condition from a 40-year-old Korean patient with liver cirrhosis. At that time, this abnormal hemoglobin was proved to have an amino acid substitution in the tryptic core fraction of α chain, but the further analysis was not preceded on account of its limited supply. Eight years afterwards (1976), this abnormal hemoglobin was happened to redetect from the same patient because he was hospitalized due to advanced liver cirrhosis. He died one year later after readmission. His mother and three of his four children are in possession of the same abnormal hemoglobin together with normal hemoglobin. The proportion of Hb Okayama and Hb A_2 Okayama in the total hemoglobin was 11.6 and 0.4 percent, respectively. Heat denaturation and Carrell's isopropanol precipitation tests were negative. Oxygen equilibrium curve of Hb Okayama showed normal capability of oxygen transport (oxygen affinity log $P_{50}=0.93$ mmHg, pH 7.4, heme-heme interaction Hill's $n=2.64$, and alkaline Bohr effect $\Delta\log P_{50}/\Delta pH=-0.43$). α Chain anomaly of Hb Okayama was reconfirmed by PCMB starch gel electrophoresis. Hb Okayama was purified by cellulose acetate membrane electrophoresis and the abnormal α chain (α^{Ok}) was isolated chromatographically. The fingerprinting of the soluble fraction of tryptic digest of α^{Ok} chain demonstrated normal scattering of the spots, therefore, the insoluble fraction (α^{Ok} core) was further digested with chymotrypsin. Fingerprint of the chymotryptic digest of α^{Ok} core indicated the appearance of an abnormal peptide located in comparison with the corresponding usual peptide. Amino acid analysis of the peptide revealed this abnormal peptide was composed of eight amino acid residues corresponding to α 110–117 peptide and a glutamyl residue at No.116 was substituted by an alanyl residue. Hb Okayama is accordingly expressed as α_2 (116 Glu→Ala) β_2 and referred to Hb Ube-4, the abnormal hemoglobin of the Korean extraction, which was reported recently by Ohba *et al.* The blood relationship between our family and Ohba's family was therefore carefully inquired giving denial results. Accordingly, Hb Okayama is concluded as a second instance of Hb Ube-4.

113. ヘモグロビン FM Osaka の発見と γ 鎖 → β 鎖転換機構の意義：林　昭・藤田富雄・山村雄一（阪大・医・三内），**藤村正哲**（淀川キリスト教病院・小児）．
Hb FM Osaka, Significance of Switching from γ to β-chain: Akira HAYASHI, Tomio FUJITA, Yuichi YAMAMURA (The 3rd Dept. Med., Osaka Univ., Osaka) and Masanori FUJIMURA (Yodogawa Christian Hosp. Pediat., Osaka)

ヘモグロビン FM Osaka 症は，われわれの開発した臨床的に重要な異常ヘモグロビン症のスクリーニング法により見出された世界で初めての胎児型 HbM 症であり，またわが国で初めての胎児型異常ヘモグロビン症である．発端者は満期安産の女の新生児で，生下時すでに著明なチアノーゼと溶血傾向が見られ，その後黄疸の増強とともに生後48時間で交換輸血が行われた．この際に得た血液を用いての検索によりまず赤血球浮遊液の酸素平衡曲線の解析から機能異常を有する異常 Hb の存在が確認され，ついで電子スピン共鳴法によりこの異常 Hb が HbM 変異種とくに non-α 鎖の遠位ヒスチジンがチロジンに置換したものであることが確定され，さらに Amberlite CG-50 を用いたカラムクロマトグラムおよびアルカリ耐性試験の結果からこの non-α 鎖が γ 鎖であることが確定した．したがって，この異常 Hb は $\alpha_2\gamma^{63\text{His}\rightarrow\text{Tyr}}$ の構造を有することが確定的で，これを HbFM Osaka と名づけた．この異常 Hb 症のきわめて興味ある点は，生体におけるヘモグロビンの γ 鎖から β 鎖への転換機構が異常 Hb の消長および患者の臨床症状に反映されていることで，すなわち交換輸血後一過性に異常 Hb の増量が見られたが，その後，生後6カ月を経た現在では異常 Hb の存在は痕跡程度で，生下時に見られた著明なチアノーゼおよび溶血徴候は完全に消失し健康な状態にある．

114. A Structural Variant of the Major Erythrocyte Membrane Protein Found in a Patient with Hereditary Spherocytosis: Takashi IMAMURA, Toshikazu MATSUO, Ikuo SUMIDA, Toshiyuki YANASE (First Dept. Med., Kyushu Univ.) **and Shunjiro KAGIYAMA** (Saga Koseikan Hosp., Saga)

We report a case of hereditary spherocytosis (HS) associated with an unusual red cell membrane abnormality detected by SDS-polyacrylamide electrophoresis. The patient, a seventeen years old woman, was referred for investigation because anemia, slight jaundice and splenomegaly were present since childhood. Hemoglobin was 7.7 g% with 18.2% reticulocytes. A peripheral blood film showed numerous spherocytes typical of HS. No abnormal hemoglobin was detected on electrophoresis, nor were there any unstable hemoglobins. From the clinical data, a diagnosis of HS was made, and splenectomy was performed. After 9 weeks, hemoglobin was 14 g%, reticulocytes 0.2%, and all the previous findings of hemolytic anemia disappeared. Although osmotically fragile erythrocytes upon incubation are persistent, subsequently the patient has been asymptomatic. On electrophoresis of the solubilized membrane proteins, the Band 3, the major protein with molecular weight of 90,000, was separated into each approximately equal amount of two distinct bands, *i.e.*, the normal Band 3 and a slightly slower moving variant with molecular weight of 94,400. No other extra band was found. The extent of phosphorylation of

the membrane substrates of intrinsic protein kinase was increased in this patient by an order of twice when whole ghosts were analysed. In contrast, the phosphorylation reaction of Band 2 and Band 3 proteins appeared to be similar, or somewhat decreased. These data indicate that more ATPs are necessary for maintainance of similar phosphorylation of proteins in the patients' erythrocytes. The molecular pathogenesis of HS remains to be clear. Elucidation of the abnormal shape transformation underlying HS not only promises to give a clue to the rational therapy for this disease, but has wider implications in biology since it could lead to a better understanding of the factors controlling the cell shape and deformability at a molecular level. The demonstration of structural alteration of the major protein in association with HS seems to be an important finding, since it may suggest the deficient function is etiologically related to the disease. Its specificity to HS should be further explored.

115. Properties of Erythrocyte Catalase in Heterozygotes for Japanese Type Acatalasemia: Masana OGATA and Junko MIZUGAKI (Dept. Public Health, Okayama Univ., Okayama)

1. Blood catalase activity in heterozygote: Investigation of the family members of Japanese type acatalasemia revealed the individuals having intermediate blood catalase activities between normal and acatalasemia, which were designated as hypocatalasemia (Takahara *et al.*, 1960). The analysis of the family pedigree with acatalasemia and hypocatalasemia cases demonstrated that hypocatalasemia is of heterozygous carrier state of acatalasemia gene. However, recent observations reported that in Swiss type acatalasemia, contrary to the Japanese type, the activity level in blood catalase of heterozygotes was found to be 65–85% of the normal level, the activity range of heterozygotes merging with that of the normals (Aebi *et al.*, 1976). In this experiment, the reconfilmation of earlier findings of heterozygotes was carried out by the determination of blood catalase activity from a through study of one kindred with Japanese type acatalasemia (GIO family). Catalase activities in hemolysates were determined by the permanganate titration methods using perborate (PU/g Hb) or hydrogen peroxide (K_{cat}) as substrate and the spectrophotometry (k/g Hb). The values measured in 3 heterozygotes by the different method amounted to 1,243.8±174.4 PU/g Hb, 1.99±0.17 K_{cat} and 106.22±18.08 k/g Hb. Average activity of normal individuals measured by the different methods amounted to 2,988.9±413.1 PU/g Hb, 4.88±0.17 K_{cat} and 321.16+60.80 k/g Hb (n=3). Comparison of the enzyme activities found in these two groups shows that no overlapping of values and a distinction between normal and Japanese type heterozygote are possible. 2. Heat stability test: The remaining relative activities were measured in partially purified catalase preparations from normal and heterozygote bloods after incubation at various temperatures

ranging from 25°C to 70°C for 10 min. No distinct difference was shown in heat stability of catalase from normal and Japanese type heterozygote. Whereas, a distinct difference was found in heat stability between normal and Swiss type heterozygote especially after 10 min incubation at 52°C, and 50% loss of the original activity was observed after incubation at 63°C for normal and at 58°C for heterozygote. Thus heat stability test evidences that biochemical characteristics of heterozygote are different from Japanese type and Swiss type. 3. SDS stability test: The remaining relative activities were measured in hemolysates from normals and heterozygotes after incubation at various concentrations of sodium dodecyl sulfate (SDS) ranging from 2–12 mM for 30 min at 25°C. SDS stability of partially purified catalase preparations from normals and heterozygotes were also examined in the same way changing SDS concentration from 0.5 mM to 3.5 mM. SDS stability of catalase from normal and Japanese type heterozygote showed no distinct difference, as examined in either hemolysates or purified catalase preparations. 4. Stability test to enzyme inhibitor: It has been shown that no distinct differences were found in stabilities to several enzyme inhibitors, such as aminotriazole, guanidine, hydroxylamine and urea, between normal and Japanese type heterozygote, as examined in either hemolysates or purified catalase preparations. 5. Comparison with Japanese type and Swiss type heterozygote: These above observations indicate the possibility to distinguish heterozygote of a intermediate specific activity but normal stability (Japanese type) or of approximately normal specific activity but low stability (Swiss type).

116. Constitutional Abnormality of Myeloperoxidase Deficiency in Leukocytes:

Masana OGATA and Junko MIZUGAKI (Dept. Public Health, Okayama Univ., Okayama)

Peroxidase deficiency in leukocytes in constitutional abnormality was reported by Grignashi *et al.* (1963) and Undritz (1966), and this deficiency in hereditary disease by Lehrer and Cline (1969). The present report describes a constitutional abnormal case, the first in Japan. The patient is a 7-year-old boy in 1978 and was diagnosed as acute bronchiolitis and detected slight anaemia at the age of 7 months. Then it was found that by the examination of his peripheral blood and bone marrow cells there was no peroxidase activity in the neutrophils and monocytes, although it was present in eosinophils and their precursors. Since then, he has been in good health despite the myeloperoxidase deficiency. The family history indicated that none of the patient's relatives had myeloperoxidase deficiency. There is no known consanguinity. In this investigation the peripheral bloods from the patient, his father, mother and sister were subjected to the morphorogical and biochemical studies. Histochemical staining by McJunkin method showed that no peroxidase activity was demonstrable in the patient's neutrophils and monocytes, although

eosinophils had the same peroxidase activity as those of normal cells. This result indicates that myeloperoxidase and eosinophil peroxidase are under the separate genetic control. In the family members, peroxidase activities were demonstrated in neutrophils, monocytes and eosinophils. The ratio of peroxidase positive cells *versus* total leukocytes representative of eosinophil activity was 1.3% in the patient, 55.0% in his father, 64.5% in his mother and 56.0% in his sister. No morphologic abnormalities were seen in the patient's neutrophils and monocytes by light microscopic examination. By electron microscopy, the granules appeared a little less in the patient's neutrophil than in the normal one and a normal configuration. Biochemical enzyme determinations on homogenates of leukocytes and hemolysates of erythrocytes were carried out. Peroxidase activity was measured by the method of Schultz *et al.* (1954) with guaiacol as substrate and demonstrated in normal leukocytes 19.66 μmoles tetraguaiacol/min/mg protein. The peroxidase activity in the patient's leukocytes was 1.88 and it was corresponded to 9.6% of the mean normal level. Leukocytes from the patient's family contained 27.9–48.6% of the mean normal peroxidase level, although histochemically this difference was not so apparent. The family studies reported here suggested that myeloperoxidase deficiency was hereditary and of an autosomal recessive mode of transmission, as reported by Lehrer and Cline (1969). The erythrocyte enzymes of the patient and his family were present in normal levels for glutathione peroxidase, superoxide dismutase, glucose-6-phosphate dehydrogenase and pyruvate kinase, but were a little lower for calatase activity than the normal, though peroxidase activity in leukocytes and catalase activity in erythrocytes were not paralleled. (Recently a part of the present results appeared in M. Ogata *et al.* 1978. *Proc. Japan Acad.*, **54:** 304).

117. ヒトにおける免疫応答の遺伝的制御 (II)：河野陽一・兼岡秀俊・太田伸生・早瀬玲子・笹月健彦 (東医歯大・難研・人類遺伝). **Genetic Control of Immune Response in Man. II.:** Yoichi KOHNO, Hidetoshi KANEOKA, Nobuo OHTA, Reiko HAYASE and Takehiko SASAZUKI (Dept. Human Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

ヒトの免疫応答の遺伝的調節機構を明らかにすることを目的として，破傷風トキソイドの免疫後の応答性を検索した結果，一般集団に非応答者が 15.2%，応答者が 84.8% 存在することが判明した．この非応答者は HLA-DHO と非常に強い相関を示すことから，HLA-DHO と連鎖不平衡にある免疫抑制遺伝子の存在が推測された．事実，非応答者の末梢リンパ球の破傷風トキソイドに対する *in vitro* での免疫二次応答を抑制する細胞の存在を明らかにし，昨年報告した．応答者の研傷風トキソイド免疫後の同トキソイドに対する応答性の経時的変化を検討した結果，一次免疫後 4 日目では応答性は認められず，14日目に強い応答性を示すことが明らかとなった．また，追加免疫を行うと追加免疫後 4 日目に一度獲得されていた応答性が低下し，14日目に再び回復してくることが観察された．そこで，一次免疫後 4 日目，および追加免疫後 4 日目の細胞を凍結保存し，それぞれ一次免疫後あるい

は二次免疫後14日目の自己の細胞に加え，破傷風トキソイドに対する免疫応答性へ及ぼす影響を検討した．この結果，一次免疫後４日目の細胞は一次免疫後14日目の細胞の示す免疫応答性を著明に抑制するが，二次免疫後14日目の細胞の示す応答性には抑制的に働かないこと，また，二次免疫後14日目の細胞は二次免疫後14日目の細胞の示す応答性を抑制しないことが判明した．これより，応答者にも免疫抑制細胞による免疫応答調節機序が存在すること，また，一次免疫と二次免疫により誘導される細胞集団は異なっていることが示唆された．

118. Genetic Analysis of HLA-D "region" (II): Nobuo OHTA, Hisamitsu UNO, Hidetoshi KANEOKA, Yoshi KOZAKI, Takehiko SASAZUKI (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo) **and Nancy REINSMOEN** (Dept. Lab. Med. and Path. Univ., Minn. Med., Minnesota)

Since HLA-D "region" is comparable to the murine H-2 I region, it is assumed that human Ir- or Is-genes would be mapped in this D "region." PLT (Primed LD Typing) reaction, MLC (Mixed Lymphocyte Culture) reaction, and B cell serology were used to analyze the genetic structure of HLA-D "region," PLT cells, which were primed against HLA-DRw2-Dw2 or HLA-DRw2-DHO haplotypes were restimulated strongly by the cells whenever they were DRw2 positive regardless to their HLA-D type. This result might indicate that PLT restimulation was caused by HLA-DR specificities and was independent to HLA-D specificities. Also this result confirmed that HLA-D specificity was different from DR specificity as we reported previously. Furthermore, HLA-DRw2-DHO homozygous cells which were primed against DRw2-Dw2 homozygous cells were restimulated significantly only by HLA-Dw2 positive cells. This finding suggested that there might be an antigen which was completely different from DR antigen but was coded for by a gene in the D "region," Subsequently HLA-D "region" was devided into at least two subregions by PLT test. Our studies, thus, showed that HLA-D was not a "locus" but a genetic "region" composed of at least two loci.

119. HLA-D Antigens in the Japanese Population (III): Masako TANIMURA, Hidetoshi KANEOKA, Nobuo OHTA and Takehiko SASAZUKI (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo)

In order to find new HLA-D antigens and in order to define the HLA system in the Japanese population, Japan HLA-D Workshop was carried out in cooperation with the 22 HLA laboratories in Japan. The analysis was performed on 220 healthy Japanese panels. Submitted 26 HLA-D homozygous cells were classified into 11 clusters, according to the mutual MLC test among them and the stimulating patterns in MLR with the panel cells. It was shown that one of the 11 clusters was Dw1 according to the MLC test with established Dw1–Dw8 typing cells originating from Caucasians. The second and the third clusters were DHO and DYT which had been already discovered in the Japanese.

The eight remaining clusters were new. Because the correlation coefficients between 11 clusters were negative and because the genotypic distribution of these clusters in the Japanese population was subjected to the Hardy-Weinberg law, it was postulated that the eight new clusters (DC1, DKT2, DSh, DEn, DHi-1, DHi-2, DNa1 and DSi) were allelic to the HLA-D antigens already known. It was found that cross reaction occurred between DHO and DC1 whose DR types were both DRw2. The total of the gene frequency of the 11 specificities and Dw2–Dw8 was 0.72. Strong linkage disequilibria were observed between every D antigen and HLA-A, B, C, DR forming the characteristic haplotypes in the Japanese population such as Aw24-B7-Dw1-DRw1, Aw24-Bw52-DHO-DRw2, Aw24-Bw54-Cw1-DYT-DRw4, 4×7, Aw33-B12-DEn-DRw6, and Aw31-Bw51-DHi-1-DRw6.

120. Association between Autoimmune Diseases and HLA-D Specificities in the Japanese Population: T. SASAZUKI, Y. KOHNO, H. KANEOKA, N. OHTA and R. HAYASE (Dept. Human Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

In Caucasians a series of autoimmune diseases such as Graves' disease, juvenile onset diabetes mellitus (JOD), myasthenia gravis (MG) and Sjögren's syndrome (SjS) have been reported to have statistical association with HLA-Dw3. We have reported that Graves' disease was associated with HLA-DHO whereas JOD had strong association with HLA-DYT in the Japanese population indicating the existence of at least two distinct genetic factors for development of the autoimmune diseases. Takayasu disease was associated with HLA-Bw52 and DHO which was in strong linkage disequilibrium with Bw52 forming Bw52-DHO haplotype. Rheumatoid arthritis had strong association with HLA-DYT. Kawasaki disease was also associated with HLA-DYT. MG and SjS, on the other hand did not show any association with HLA-D specificities. HLA-Dw3, which was not observed in the healthy Japanese population, was found around 10% (7.5–18.3%) of the patients with either JOD, Sjögren's syndrome, MG, or Takayasu disease. Our recent finding of the complete association between immune responsiveness to certain antigen and one of the B cell aloantigens coded for by a gene in the HLA-D region seems to suggest the existence of HLA-linked immune response genes and their crucial roles in the pathogenesis of HLA-associated autoimmune diseases in man.

121. Rheumatic Fever and HLA Antigens: Kenji NARITOMI, Hiroshi MIYAZAKI and Koichiro MIYATA (Dept. Pediat., Kagoshima Univ., Kagoshima)

Through study of experimental carditis using monkeys we suggested streptococcal M protein (Lancefield's method) and/or its immune complex play a main role as the patho-

genesis of rheumatic fever (RF). And here we studied its disease susceptibility by means of HLA typing. (1) Subjects and method: 29 cases of RF who fulfilled with revised Jones criteria (1965) and 57 controls were examined according to standard microdroplet lymphocytotoxicity test about 10 A locus and 13 B locus antigens. (2) Results: 1) BW35 was significantly increased in RF compared with control (RF 44.8%, control 10.5%, $\chi^2=11.222$, $p<0.023$, R.R.=6.1); 2) B5 was decreased but not significantly (RF 20.7%, control 42.1%); 3) AW24 was decreased but not significantly; 4) There was no difference on other antigens; 5) There was no difference between RF with or without carditis. Increased frequency in RF was already reported by Leirisalo *et al.* in Finland (1977), and it is very interesting from the humangenetic point of view that the same associated antigen in RF was disclosed in Finland and Japan.

122. Studies on the Immunogenetic Factors in the Pathogenesis of Acute Poststreptococcal Glomerulonephritis (I): Yasuharu NISHIMURA, Reiko HAYASE, Takehiko SASAZUKI (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo), **Itsuo IWAMOTO** (2nd Dept. Int. Med., Chiba Univ., Chiba), **Hiroki TSUCHIDA** (Dept. Int. Med., Chiba Shakai Hoken Hosp., Chiba) **and Osamu KOHASHI** (Microbiol. Tokai Univ., Isehara)

Acute poststreptococcal glomerulonephritis (APSGN) is known as a immune complex disease and occurs after infection of group A type 12 hemolytic streptococcus. In the pathogenesis of the APSGN, streptococcal infection might be one of the most important environmental factors. As genetic factors, on the other hand, immune responsiveness to the streptococcal antigen might be directly involved in developing APSGN. In order to get a clue to reveal immunogenetic factors in developing the APSGN, we selected 46 Japanese patients with APSGN and typed for their HLA-A, B, C and D antigens. A significant increase in frequency of HLA-B12 in the patient group was demonstrated (relative risk=3.5, $p<0.02$). Subsequently we observed a strong association of the patient group with HLA-DEn (relative risk=9.0, $p<0.01$), which is a new HLA-D specificity and in strong linkage disequilibrium with HLA-B12 in the Japanese population, than with HLA-B12. A primary association of the patients with APSGN was thus with HLA-DEn, and increased frequency of HLA-B12 in the patient group was most likely due to the linkage disequilibrium between HLA-B12 and HLA-DEn. Because HLA-D region is comparable to the I region of murine H-2 complex, it might be reasonable to assume that there would be an Ir or Is gene which is in strong linkage disequilibrium with HLA-DEn determining the susceptibility to APSGN by controling the immune responsiveness of the host to a particular antigeneic determinant of the nephritogenic streptococci. We then examined the association between HLA specificities and immune response to the water

soluble fraction of group A type 12 streptococcus *in vitro* in 57 healthy Japanese. The population was devided into responders and non-responders. There was increased frequency of HLA-B15 among responders ($p<0.01$). Further study is now undertaken to show the clinical relevance of this type of immune response to streptococcal antigens.

123. Immunogenetical Analysis on Hepatitis B Virus-Host Reaction: Hidetoshi KANEOKA, Takehiko SASAZUKI (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo) **and Makoto MAYUMI** (Hepatitis Div., Tokyo in Metropol. Inst. Med. Sci., Tokyo)

Hepatitis B Virus (HBV) is thought to play important roles in developing liver cirrhosis and primary hehatoma as well as viral hepatitis. After infection with HBV, it is well known that human beings shows three different ways in responding against the HBV, namely 1) immediate elimination of HBV by producing anti HBV antibody, 2) slow elimination after long carrier state, or 3) eternal carrier state. From the standpoint of antibody production, there are three patterns in man: 1) producing both of anti HBs antibody and anti HBc antibody, 2) producing one of them, or 3) producing none of them. For the purpose of genetic analysis on immune response to HBV and the resolution of its clinical importance, we examined the association between the presence of HBV antigens and antibody against them and HLA system in healthy population. Thirty nine out of 195 healthy men (20.0%) with anti HB antibodies (anti HBs antibody and/or anti HBc antibody) showed the strong association with HLA-Bw35 ($p<0.005$). Moreover 26 men with anti HBs antibody and 28 men with anti HBc antibody also showed the association with HLA-Bw35. These results seem to indicate that immune response to HBV might be under the genetic control in man.

124. A Study on Pathogenesis of Hydatidiform Mole by HLA Marker: Koso OHAMA (Dept. Obst. Gynec., Hiroshima Univ., Hiroshima) **and Yasuhiko FUKUDA** (Dept. 2nd Surg., Hiroshima Univ., Hiroshima)

It is well known that complete or classic mole exclusively shows a normal female karyotype, 46,XX. Recently Kajii and Ohama analyzed heteromorphic chromosomes of molar cells and their parental lymphocytes using fluorescence Q and R-band techniques, and revealed that homologous chromosomes of the mole were homozygous which were inherited from one of the two paternal homologous chromosomes. Subsequently, similar data were independently reported by Wake *et al.* and Jacobs *et al.* These findings suggest that androgenesis is a cause of a complete mole. However, there still remain two possibilities in the occurrence of such chromosomal homozygosity. One is by fertilization of normal haploid sperm followed by duplication of its chromosomes without cytokinesis,

and the second is by fertilization of diploid sperm formed at the second meiotic division. It has been pointed out that variants of certain isozymes or HLA typing may be useful in the discrimination between these two possibilities as adopted in ovarian teratomas. From this view point, we have attempted to analyze HLA typing of moles and their parents. Moles obtained from 12 patients for the study were divided into two groups; complete mole and partial mole with coexistent fetus. Molar specimens were rinsed in normal saline solution to avoid contamination of maternal tissues, finely minced and then cultured in two separate flasks containing Eagle's minimum essential medium with 20% calf serum. When the adequate cell growth was observed, cells were trypsinized and collected as the cell suspension. The cells thus collected and the lymphocytes of peripheral blood from their parents were used for HLA determination. HLA typing for A and B loci was made by two stage microcytotoxicity test according to the NIH standard method with 118 antisera. Paralleling HLA typing, chromosome heteromorphism was also examined by Q-band technique. Result of HLA typing of 10 complete moles and their parents are as follows. There was no case in which molar cells possess two antigens either for A locus or for B locus, whereas different types of antigens for each locus were detected in the parents. In 3 cases, neither of the two antigens for A and B in maternal lymphocytes could be detected in the mole, and the antigens which molar cells possessed were similar to one of the two paternal antigens. Similar findings for either of A and B loci were obtained in 5 cases. In remaining 2 cases, unfortunately, no informative data were provided, because the number or the type of antigens determined in mole and/or parents was inadequate for analysis. The results of chromosome heteromorphism analyses showed that all these complete moles were paternal in origin. On the other hand, chromosome constitution of two partial moles were detected to be heterozygous and maternal in origin for one haploid set by analyses of HLA and chromosome heteromorphism, while their karyotype was 46,XX. Although there are no data on the frequency of crossing-over between HLA loci and the centromere of chromosome 6, these observations strongly indicate that complete mole arises through the process of fertilization by haploid sperm of 23,X which subsequently duplicates without cytokinesis, and that a partial mole develops from a usual zygote.

125. 染色体異常胎児の皮膚紋理分析（第2報）ダウン症以外の常染色体異常胎児について：鈴森 薫・小石多紀子・八神喜昭（名市大・産婦），大石英恒（愛知コロニー）. **Dermatoglyphic Features of the Fetuses with Chromosomal Aberration. 2nd Report: Autosomal Anomalies except Down's Syndrome:** Kaoru SUZUMORI, Takiko KOISHI, Yoshiaki YAGAMI (Dept. Obstet. Gynec., Nagoya City Univ., Nagoya) and Hidetsune OISHI (Aichi Collony)

岡島による胎児皮膚紋理分析法は画期的なものであり，われわれ産科医が近年開発しつつある胎児

診断学の立場から応用できる可能性を秘めているのではないかとの考えのもとに，皮膚紋理学上その特徴が明らかな染色体異常に着目し，染色体異常胎児の皮膚紋理分析を進めている．ダウン症胎児については，先回の本学会総会にて発表しているので，今回はその他の染色体異常胎児について報告した．第1の症例は，羊水胎表造影上の所見よりE-トリソミーと診断し，羊水培養細胞にて確診した妊娠33週の中絶胎児である．手指の異常として，左側において拇指の遠位付着，第2指の屈曲拘縮が強度で変形しており，手掌部では，近位側，遠位側横走屈曲線は形成されているものの縦走屈曲線は欠如していた．E-トリソミーに特徴的な紋様としては，指頭における弓状紋の高頻度出現，右手拇指頭の橈側蹄状紋，両手第5指の単一屈曲線，Distal axial triradius が観察された．なお，全指総隆線数は39であった．第2の症例は，5p−; 16q+ の相互転座保因者より中絶された妊娠25週の 5p− の女児である．本症例において 5p− であることを示す特徴的紋様として，指頭紋型で見られた渦状紋の高頻度の存在，右手拇指球部の紋理形成，第4指間の蹄状紋，小指球部紋様の欠如が挙げられる．なお，全指総隆線数は129であった．本法による胎児皮膚紋理分析は，詳細な点まで解析可能であり，染色体異常が疑われる胎児の診断には有効な方法であることが示唆された．

126. Ridge Counts in the Hallucal Area of Twins: Akio ASAKA (Inst. Brain Res., Univ. Tokyo, Tokyo) **and Michio OKAJIMA** (Dept. Forens. Med., Tokyo Med. Dent. Univ., Tokyo)

Ridge counts were examined in hallucal areas in 176 pairs of twins, consisting of 140 monozygotic (MZ) and 23 same-sexed and 13 opposite-sexed dizygotic (DZ) twins. Subjects are those included in "Tokyo 12-year Twin Registration" from 1969 to 1977. The zygosity of these twins was determined with the aid of blood groups and anthropological examinations. Hallucal patterns were classified into *Loop distal, Whorl, Loop tibial, Arch fibular, Arch tibial* and *Arch proximal.* Neither sex difference not laterality in the frequency of patterns was recognized. Patterns of *Loop distal* and *Whorl* were seen in 588 (83.5%) out of 704 soles examined. Ridge counting between the core of patterns and *f* triradius was made in the above two patterns, and the intraclass correlation coefficient within the pairs was calculated. Correlation coefficients in the *Loop distal* and *Whorl* combined, when they were present in both soles, were 0.849 (both soles), 0.793 (left sole), 0.754 (right sole) in MZ(N=98), and 0.638(b), 0.545(l), 0.646(r) in DZ(N=18). Correlation coefficients in the *Loop distal*, being concordant in both soles, were 0.874(b), 0.836(l), 0.811(r) in MZ(N=54), and 0.485(b), 0.496(l), 0.440(r) in DZ(N=5). Correlation coefficients in the *Whorl*, being concordant in both soles, were 0.815(b), 0.831(l), 0.612(r) in MZ(N=24), and 0.765(b), 0.386(l), 0.923(r) in DZ(N=3). The majority of these correlation coefficients were higher in MZ than in DZ, and both values in MZ and DZ were significantly higher than zero, indicating that the ridge count in the hallucal area is under genetic control.

127. 胎児皮膚隆線の検査法改良と初期分化：岡島道夫 (東医歯大・法医). **A Revised Examination Method and Initial Differentiation of Fetal Dermal Ridges:** Michio OKAJIMA (Dept. Forens. Med., Tokyo Med. Dent. Univ., Tokyo).

1975年に岡島が発表した検査法を改良し，14週前後の胎児の検査に適した方法を確立した．ホルマリン固定標本に 3% KOH 溶液を作用させる点は同じであるが，作用時間を15時間に延長し，2回作用させる点で異なっている．1回目のアルカリ処理後ブラシをかけて表皮の表層部を除去した後，再度アルカリ処理をしてブラシをかけると真皮が容易に露出する．綿棒の代わりに縫針の耳に太目の絹糸で結び目を作り，糸の断端をブラシとして使用すると，小さな標本では具合がよい．真皮はトルイジンブルーで染色する．隆線の分化は，紋理のある部位では紋理の中心部から始まる．隆線の突出部は紫色に染色されるが，溝の部分，すなわち将来汗腺管の通る部分はほとんど染まらない．他方，母指球，小指球，足底の近位側部などのように紋理形成の弱い所では，隆線分化は散在性に出現し，それらが拡大癒合して全表面を覆うようになる．Bonnevie (1927) と Schaeuble (1933) は連続組織切片標本を用いて隆線分化の進行順序を観察しているが，三叉部で遅れることを記載している．今回の直接の表面観察によって，この事実を確認することができた．新しい興味ある知見として，隆線の分化が始まる前の時期に，真皮表面にチリメン状に染まる構造が出現していることが見つかった．この構造は，将来この部に出現すると予想される隆線の紋様を浮き出した感じで，とくに足紋指間部ではパッドの形態によく一致していた．この事実から，皮膚紋理の基本的形態は，隆線分化の開始よりもかなり早い時期に決定されているものと推測される．

128. Dermatoglyphs in 37 Colourblind Males: M. HAYASHI (Shinkawabashi Hosp., Kawasaki) **and S. De Bie** (Center Med. Genet., Univ. Ghent, Belgium)

Protan and deutan-types of congenital colourblindness both are X-linked recessive diseases and the alleles are at the same locus. In Japan, about 4% of males are affected with these anomalies. Digital and palmar patterns of 37 colourblind male (6 protan and 31 deutan) were examined in the finger pattern type, direction of the pattern, total finger ridge count, pattern intensity, pattern frequency in different palmar areas, main line terminations, position of the axial triradius and a-b ridge count. Comparison of the results with those of a control group consisting of 52 males, living in the same area, revealed only very small differences. In the protan group, a slight increase of both ulnar and radial loops was found on the fingers; on the palm the axial triradius was more often displaced distally and in the left hypothenar a decrease of real patterns was observed. In the deutan group, patterns were more frequently observed in III interdigital area and the main line C was more often absent or abortive on both hands, while on the left hand a decrease of hypothenar patterns was found. However, none of these differences were significant at the 0.05 level. We want to express our thanks to Prof. Matsuo and his staff for giving us opportunity to take fingerprints.

129. Digital and Palmar Dermatoglyphs in Retinoblastoma: M. HAYASHI (Shinkawabashi Hosp., Kawasaki) **and S. De Bie** (Center Med. Genet., Univ. Ghent, Belgium)

As the retinoblastoma occasionally associates with congenital malformations or mental retardation and as a small chromosomal deletion was described in a retinoblastoma patient without mental retardation or other somatic anomalies, digital and palmar dermatoglyphs were analyzed in 36 non-related retinoblastoma patients, 22 males and 14 females. Comparison of the dermatoglyphs of the 22 male retinoblastoma patients with those of 280 male controls showed a slightly increased TFRC, a higher whorl frequency and a decreased frequency of radial loops on the fingers; on the palm main line C tends to be more often absent or abortive, while main line A is more transversal. In the female retinoblastoma patients, as compared to 281 female controls, an increased frequency of arches together with a decreased frequency of ulnar loops were observed on the fingers. The a-b ridge count was increased and patterns were more frequently found in the different palmar areas. In both, male and female patients, however, none of these differences were significant at 0.05 level.

130. Dermatoglyphic Study on Hypoplastic Thumbs: Takashi SUZUKI, Kokichi TSUCHIYA (Dept. Orthop. Surg., Yokohama City Univ., Yokohama) **and Ichiro MATSUI** (Kanagawa Child. Hosp., Yokohama)

A dermatoglyphic study was carried out on 10 persons affected with hypoplastic thumbs in 16 hands and 84 persons with other hand anomalies in 119 hands. Controls were 1,026 healthy children. The hypoplastic thumbs were classified into five degrees from thenar muscle atrophies to total absence of thumbs according to the Blauth' classification. The dermal ridge patterns were analyzed according to the Penrose' memorandum. 1) In the cases with hypoplastic thumbs, higher incidences of high axial triradii, radial loops, simian creases and first interdigital patterns were noted. 2) Higher degrees of the *atd* angle were observed in accordance with the severity of the hypoplasia of the thumb. 3) There were one case of the floating thumb and three cases of the total absence of the thumb and all of them lacked in axial triradii. 4) In cases of finger nubbins with rudimental thumbs, no axial triradii were found, whereas in cases of finger nubbins with almost normal thumbs, axial triradii were found. Thus, the absence and higher position of the axial triradius associate with the grade of hypoplasia of the thumb, and the axial triradius is considered to be the digital triradius of the thumb.

131. 足底母指球紋の変異型について：松井一郎（神奈川こども医療センター）. **Minor Variations in Hallucal Patterns on Sole:** Ichiro Matsui (Kanagawa Child. Med. Center, Yokohama)

足底の母指球紋はダウン症候群 (A^t), 13トリソミー症候群 (A^f, L^t) などで診断上重要である．この部の紋型は手掌小指球部とならんで，紋様が最も変化に富む．足底母指球紋型については細部の規定がなく，定量的判断も不可能である．加えて隆線走行の種々のバリエーションが多く，基本紋型が多くの修飾をうけている．このため紋型の判断に迷う場合が少なくない．そこで，正常個体の足底母指球紋の変異の範囲を知る目的で分析を行った．対象はきょうだいを除外した1,026名（男523, 女503）の健康学童．分類の基本は Cummins を参考にして記載した．1) Open field, 2) Arch 型 (A^t, A^p, A^f, TA), 3) Loop 型 (L^d, L^t, L^f, L^p), 4) Whorl 型 (W, LP, TL, CP^d, CP^t, CP^f, CP^p, その他の W) の4群に分けた．また seam, fan, pocket などの変異型を記載．正常個体で変異が最も多い紋型は A^t 型であった．定型的 A^t（ダウン症にみられるような）の頻度は男子 4.8%，女子 1.4% であった．これに対して顕著な fan, seam, pocket などを有する変異型の頻度は男 7.5%，女 2.9% と2倍近い頻度であった．他方，ダウン症候群では変異型の頻度は顕著に低かった．

学会記事 Newsletter

日本人類遺伝学会評議員改選

日本人類遺伝学会評議員は，改選により，昭和54年，55年の2か年間，下記の100名の会員に委属された．（昭和54年6月10日）

相沢　幹（北大・医・病理）
赤石　英（東北大・医・法医）
浅香昭雄（東大・医・脳研）
阿部達生（京都府立医大・公衆衛生）
有馬正高（武蔵療養所神経センター）
阿波章夫（放射線影響研，広島）
粟野亥佐武（福島県環境医学研）
井形昭弘（鹿児島大・医・内科）
池内達郎（東医歯大・難研）
石原隆昭（放射線医学総合研）
井関尚栄（科警研）
一戸喜兵衛（北大・医・産婦人科）
井上英二（東大・医・脳研）
今泉洋子（厚生省人口問題研）
遠藤晃（山形大・医・衛生）
大浦敏明（大阪市立小児保健センター）
岡島道夫（東医歯大・医・法医）
岡本直正（広島大・原放医研）
荻田善一（富山大・和漢薬研）
大倉興司（東医歯大・難研）
大堂庄三（宮崎医大・小児科）
大野文俊（徳島大・医・内科）
尾本恵一（東大・理・人類）
梶井正（山口大・医・小児科）
亀山義郎（名大・環境医研）
川井尚臣（徳島大・医・内科）
菊池康基（武田薬品・中央研）
北川照男（日大・医・小児科）
木田盈四郎（帝京大・医・小児科）
木村資生（遺伝研・集団遺伝）
工藤昭夫（九大・理・数学）
黒岩義五郎（九大・医・神経内科）
黒木良和（神奈川県立こども医療センター）
小西俊造（山口大・学長）
古味信彦（徳島大・医・外科）
近藤恭司（名大・農・家畜育種）
近藤喜代太郎（新潟大・脳研）
後藤由夫（弘前大・医・内科）
堺俊明（大阪医大・精神）
佐々木正夫（京大・放射線生物研）
佐々木元資（長崎大・医・口腔基礎医学）
佐々木本道（北大・理・動物染色体研）
笹月健彦（東医歯大・難研）
塩見敏男（長崎大・医・原医研）
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武部啓（京大・放射線生物研）
田島弥太郎（遺伝研）
多田啓也（東北大・医・小児科）
田中克己（東医歯大・名誉教授）
千代豪昭（兵庫医大・遺伝）
辻義人（福島医大・公衛）
寺脇保（鹿児島大・医・小児科）
外村晶（東医歯大・難研）
中込弥男（遺伝研・人類遺伝）
中島章（順天堂大・医・眼科）
中鳩八良（東医歯大・医・法医）
中島照（東医歯大・難研）
西村秀雄（実験動物中央研）

錬 石 昇太郎（放射線影響研・長崎）
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支 倉 逸 人（埼玉医大・法医）
埴 村 和 郎（東大・理・人類）
半 田 順 俊（和歌山医大・解剖）
馬 場 一 雄（日大・医・小児科）
日 暮 真（東大・医・母子保健）
平 山 宗 宏（東大・医・保健）
福 島 務（福島医大・産婦人科）
福 山 幸 夫（東京女子医大・小児科）
藤 木 典 生（愛知心身障害コロニー・発達障害研）
藤 田 弘 子（大阪市大・生活科学）
古 川 研（馬群大・医・法医）
古 庄 敏 行（鹿児島大・医・衛生）
古 屋 義 人（産業医大・法医）
古 山 順 一（兵庫医大・遺伝）
増 田 正 典（京都府立医大・内科）
松 井 一 郎（神奈川県立こども医療センター）
松 田 健 史（富山医薬大・医・解剖）
松 田 博（愛媛大・医・小児科）
松 永 英（遺伝研・人類遺伝）
松 本 秀 雄（大阪医大・法医）
美 甘 和 哉（旭川医大・生物）
三 木 敏 行（東大・医・法医）
満 田 久 敏
三 村 悟 郎（琉球大・保・内科）
宮 尾 益 英（徳島大・医・小児科）
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三 好 和 夫（徳島大・医・内科）
三 輪 史 郎（東大・医科研）
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安 田 徳 一（放射線医学総合研）
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山 野 利 尚（徳島大・内科）
山 村 雄 一（大阪大・医・内科）
山 本 茂（科警研）
渡 辺 厳 一（新潟大・医・衛生）

会計担当幹事の委嘱

本学会第23回大会のときの承認により，理事に就任した外村晶会計担当幹事の後任として，今般，池内達郎会員に幹事を委嘱することになった．

国際医学教育コース「赤血球の遺伝性疾患」の開催について

日 時：昭和55年1月21～26日
場 所：Kauai Surf Hotel（米国カウアイ島リフエ市）
登録料：395.00ドル
内 容：赤血球の生成と調節（Goldwasser, Nienhuis, Takaku, Krantz）
赤血球膜（Shohet, Yawata），赤血球酵素（Valentine, Tanaka）
異常ヘモグロビン（Lehmann, Rucknagel, Schneider, Carrell, Powars）
サラセミア（Wasi, Kan, Bessman）
遺伝性赤血球疾患の出生前診断（Bowman, Kan）
後 援：シカゴ大学病理，東京大学医科学研究所内科
参加お問合せ先：〒108 東京都港区白金台東京大学医科学研究所内科
三輪史朗（電話 03-443-8111，内線 350）

投 稿 規 定 (1976年6月改訂)

投稿者の資格　本会会員による投稿が優先されるが，会員外の共著者を含むことは差しつかえない．

論文の種類　原著を主とする．他にとくに優れた総説，および人類遺伝学の研究に有用な資料を掲載する．他の刊行物に掲載された論文は受付けない．

原稿の部数　2部

用語　十分に推敲された英語，ドイツ語，またはフランス語が望ましい．

本文の用紙　A4判，またはこれに最も近い大きさの厚手の用紙．

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原稿の表紙　表紙にはタイトル，著者名，所属機関名とその所在地のみを欧文と和文で記載する．本文は第2ページから書きはじめる．

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例：Dahlberg, G. 1950. Methods for population genetics. *Am. J. Biol.* **25**: 90-104.

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