一 般 講 演 General Contribution

1. **Yoshihiro KINOSHITA** (Keio Kenko Sodan Center, Tokyo), **Aya HORIGUCHI** (Dept. Obst. Gyn., Dokkyo Med. Col., Tochigi), **Michitsugu SEO** (Shō Hosp., Tokyo) **and Shozo TAMURA** (Dept. Obst. Gyn., Univ. Keio, Tokyo): **A Case of Primary Amenorrhea with (X; 21) Translocation.**

A patient complaining of primary amenorrhea with balanced X-autosomal translocation, 46, X, t(X; 21) (q13; p13) was presented here. She was 22-year-old woman with neither overt congenital malformations nor mental retardation, but showed undeveloped secondary sexual characters,—flat breast, scanty pubic and axillary hair, infantile external genitalia, and so on. Peritoneoscopic examination revealed a hypoplastic uterus and almond-shaped streak gonads. Hypogonadism and hypopituitarism were suspected from hormon assays of urine and serum.

Late replicating X chromosome was identified to be morphologically normal X chromosome, not translocated one, by both autoradiography and BUDR-acridine orange methods. Several cases with active X-autosomal translocation previously reported showed almost the same symptome as the primary amenorrhea, while other reported cases with inactive X-autosomal translocation showed various phenotypes. We discussed the significance of the wide distribution of break point in these cases.

2. **T. MOTEGI, M. KAGA** (Dept. Pediat., Branch Hosp,. Tokyo Univ., Tokyo), **H. AOKI** (Dept. Cytogenet., Med. Res. Inst., Tokyo Med. and Dent. Univ., Tokyo), **Y. ATAKA and A. ASAKA** (Dept. Hum. Genet. and Criminol., Brain Res. Inst., Tokyo Univ., Tokyo): **Two Cases of Macrocrania with a Extra Small Acrocentric Chromosome.**

Chromosome analysis with a Giemsa banding technique was performed in a female infant of 6 months old who had normal somatic growth, psychomotor retardation (D.Q. 52), hypotonia, macrocephaly and many minor anomalies. Her karyotype was 47, XX, +mar and not mosaic. The marker chromosome was a satellated acrocentric one with the size of G group and a dark band at the distal terminal of the long arm. The centromere was dark, but not so as chromosome 22. The identification of the marker chromosome was impossible, because her parents were cytogenetically normal and the marker was too small. EMI-Scan. of the head and PVG revealed the normal ventricular system. Metabolic disorders

were denied by the assay of the various lysosomal enzymes of white blood cells, blood lipid, urine amino acids and so on.

Another case was 16-year-old boy who had mental deficiency (mental age: 9 m), uncontrollable seizures, increase of the total head height and head circumference and many minor anomalies. His karyotype was 47, XY, +mar and not mosaic. The marker chromosome was a satellated acrocentric one of G-group-sized. Two dark bands were found at the intermediate portion and distal terminal of the long arm. His father was dead 7 years ago and his mother was of normal karyotype. Therefore, identification of the marker chromosome was impossible. Screening tests for metabolic disorders by urine were all within normal limits. No roentgenologic changes were found except the mild callvarial thickening probably due to diphenylhydantoin medication. Skull changes in the chromosomal aberrations has been confined to microcephaly in most cases and macrocephaly has not been described. Our two cases are interesting because of the chromosomal aberrations with macrocephaly and different markers to each other.

3. **Tomoko SHIMA, Ryuichi TSUKINO, Hirotoshi SUGINO, Hiromi SAKAI and Teisuke KODAMA** (Dept. Pediat. Wakayama Medical College, Wakayama): Cri du Chat Syndrome with Balanced B/C Translocation in Sister, Mother, and Grandfather.

Y.S., a 8-day-old male infant born 5. Nov. '75 to 27-year-old mother and 29-year-old father. Pregnancy was uncomplicated. Gestation period was 42 weeks. Delivery was performed with oxitocin injection. Birthweight was 3,100 g and height was 48.0 cm. Apgar score was complete. His cry was weak and highpitched, comparable to the mewing of a cat, which had persisted.

Physical examination at hospitalization: Weight 2,924 g, height 46.6 cm and head circumference 32.7 cm. He was so-called round-faced infant with slight microcephaly and micrognathia. Eyes were almond-shaped, palpebral fissures were slightly oblique with epicanthal folds. Ears were low-set and a accesory auricle in right side. Cleft lip was present at the right angle of the mouth. Palate was high-arched. Short neck and excess skin at back of the neck were present. Simian line was noted on the left hand. Deep tendon and superficial reflexes were present but the lower extrimites showed scissors phenomenon with rigidity. No heart murmers were present.

Other examinations: Mild anemia [RBC: 339×10^4/cmm, Hb: 13.6 g/dl], slightly high CPK [111 mU] and LDH [446 mU] were seen. EEG and ECG were in normal range. Brain echography revealed no midline-shift and ventricle dilatation. Ocular

fundi were normal but the vitrous bodies of both sides had mild opacity. Larynx was normal with X-ray photography and indirect laryngoscopy.

Family history: Both parents are in good health. There are a 15-month-old sister and one miscarrage at 3 months. The mother had one sister, who died at 10 years of age from acute enteritis. She had round face and weak, high-pitched cries and never walked. Two other pregnancies ended in artificial abortion at 9 months and spontaneous abortion at 3 months. The maternal grandfather had 9 sibs and 5 of them died at less than 10 months of age. One living sister has no children and one miscarrage.

Chromosome studies: Analysis was performed on lymphocyte cultures grown and treated in standard manner. Further karyotype analysis using both G-banding and C-banding were carried out.

Patient	46, XY, del (5) (p13)
Sister	46, XX, t (5; 6) (p13; q27)
Mother	46, XX, t (5; 6) (p13; q27)
Father	46, XY
Maternal grandfather	46, XY, t (5; 6) (p13; q27)
Maternal grandmother	46, XX

Patient went back home at 4 weeks of age. On 26. Jan. '76, he could not suck well and suddenly showed dyspnea and died on 29. Jan. '76. The autopsy was not allowed.

This case may be the first report of reciprocal translocation involving the short arm of No. 5 chromosome and the long arm of No. 6 chromosome.

4. **大浜紘三**（広島大・産婦人科）：**ヒト染色体の多型による卵巣奇形腫の発生機序検討の試み.** Kozo OHHAMA (Dept. Obst. Gynec., Hiroshima Univ., Hiroshima): **Chromosomal Polymorphisms in Human Ovarian Teratomas.**

卵巣奇形腫および胎児性癌はいずれも胚細胞由来の腫瘍と考えられているが，詳細については不明な点が多い．一方ヒト染色体の多型は個人識別やトリソミーの発生機序解明等に極めて有用である．そこで卵巣の類皮嚢胞腫2例，充実性奇形腫2例，胎児性癌2例，計6例の腫瘍組織培養，および宿主末梢リンパ球培養を行ない，quinacrine 染色による染色体の多型を分析し，腫瘍発生機序の検討を試みた．

類皮嚢胞腫の1例は 47, XX で No. 14, 21, 22 の染色体が heterozygous で，他の例は 46, XX であったが No. 3, 13, 15 が homozygous であった．充実性奇形腫の第1例は 46, XX で，No. 13, 21 が，また acridine orange 染色で No. 22 が homozygous であったが，第2例は 48, XX, +14, +21 で No. 15, 21 の多型は heterozygous を示した．胎児性癌の2例は，培養標本でいずれも 46, XX の核型を示し，リンパ球と同じ多型を示したため宿主側の細胞の混入の可能性が残るが，1例での直接標本では No. 21 が heterozygous の組合せであった．

性腺，特に睾丸奇形腫の性染色質検査を行った Theiss らの結果からは，奇形腫は第1，第2減数分裂を終え haploid となった性細胞が2個合体して発生すると推測されるが，今回と同様染色体の多型等を指標とした Linder らの類皮嚢胞腫の成績は，第1減数分裂を終えた細胞から生じ，それは第2減数分裂の抑制または第2極体の取り込みといった機序を示唆している．しかし今回の成績は，第1減数分裂の前および後の細胞のいずれからも生じることを示したが，独立した haploid の性細胞（卵子）の合体による発生機序は否定的であった．

5. **Yoshifumi YAMAMOTO, Yuko ENDO and Yoshikazu KUROKI** (Div. Med. Genet., Kanagawa Children's Medical Center, Kanagawa): **A Case of X-Autosome Translocation.**

KC-17734, a 3-years-old girl with partial trisomy 17 (pter→q21) and partial monosomy X(pter→q13), daughter of mother with a balanced reciprocal translocation [46, X, t (X; 17) (q13; q21)] is presented.

Clinical findings were mental defficiency, short stature, prominent forehead, antimongoloid slanting, corneal opacity, beaked nose, high arched palate, short neck, pectus excavatum, adducted thumbs, low total finger ridge count, high axial triradius and bilateral third interdigital loop. Pneumoencephalogram revealed dilated lateral ventricles and electroencephalographic study showed sporadic spike and wave complex in the central area without clinical seizure. Other laboratory data including thyroid function and growth hormone secretion test were all within normal limits.

She expired at 3 years and 4 months with acute pneumonia. Postmortem examination showed streak gonad, probably due to partial monosomy of X. Uterus and Fallopian tube seemed to have normal histological constitution.

Two other reported cases of partial 17 trisomy were compared, and main clinical features of partial 17 trisomy (pter→q21) seemed to be antimongoloid slanting, low set and malformed ears, high arched palate, beaked nose and finger joints contracture.

If 17 trisomy zygote is fatal, translocated X may save this serious condition by random inactivation resulting partial 17 trisomy mosaic state. Disappointedly the lack of autoradiographic study could not clarify the problem.

〔**質問**〕 **古山順一**（兵庫医大・遺伝）：Duplication/deficiency syndrome の症例では，serious な染色体異常の臨床像が，片方の臨床像をかくすといわれているが，本症例で Xp-(Turner's syndrome) phenotype と 17p trisomy phenotype はどのように表現されているか．

〔**答**〕 **山本佳史**：ターナー症候群でもみられる症状を除くと，先ほど述べたように，目じりが下り，鼻根が比較的高く，鼻はさく口嘴状である，といった顔貌の特徴と，強度の発育・発達障害ぐらいしか残らない．

〔**質問**〕 **柳沢　慧**（山口大・小児）："Small" X-chromatin の判定基準について．

〔答〕 **山本佳史**：核膜に接しているもので，他の核質のクロマチンがその大きさを超えないもの，としたが，計測して判定しているわけではないので，御指摘のようにXクロマチンであるという確証はない．

6. **外村　晶・青木裕子・岸　邦和・斉藤深美子・浦野明子**（東医歯大・難研・細胞遺伝）：**日本人の末梢血リンパ球にみられる染色体異常**．Akira TONOMURA, Hiroko AOKI, Kunikazu KISHI, Fumiko SAITO and Akiko URANO (Dept. Cytogenet., MRI, Tokyo Med. Dent. Univ., Tokyo): **Chromosome Aberrations Found in Lymphocytes from Healthy Japanese Persons.**

本研究は，環境汚染，とくに原発開発などによる低線量放射線のヒトへの危険度を推定するための基礎的研究の1つとして，現在の日本人集団の末梢血リンパ球における染色体異常の種類と頻度を調査し，その平均的値を把握することを目的としている．年齢による影響を考慮し，20～60歳までの10歳階級別に対象者を選び，そのなかから胸部X線撮影以外の被曝歴を有しないものを選定した．しかし，高年齢層の場合は，過去に胃検査などのためにX線照射を受けた経験を有するものもふくまれている．末梢血培養は，すべて50時間培養で，第1回目の分裂中期像について，1人平均 1,000 細胞（男16名，女17名），計 31,003 細胞を観察した．解析は写真分析法によった．

染色分体型異常に関しては，年齢による差異は認められなかったが，染色体型異常は高年齢になるにつれて増加し，とくに Dic.+Ring の出現頻度は 50～60 歳代にかけて高くなった．なお，年齢を除外した1細胞当りの染色体異常の出現頻度は，Breaks 1.00%，Iso-breaks 0.37%，Exchange 0.13%，Dic. 0.11%，Ring 0.004%，Monocentric 0.05%，Translocation 0.04% そして Fragments 0.2% であった．

一方，染色体の数的異常も観察され，とくに過剰染色体を1個もつ染色体数47の細胞に注目して分析を行った．その結果，47-細胞の出現頻度は年齢とともに増加することが明らかになった．そして，染色体不分離は各染色体について任意ではなく，X染色体とG群の染色体によるものが多く認められた．したがって，47-細胞の増加は男よりも女において顕著であった．

〔質問〕 **阿波章夫**（放影研・広島）：1) 50時間培養の場合，X_2 細胞の割合はどの程度あったか．2) Derived chromosome-type の異常の頻度が高年齢群に多かったか．

〔答〕 **外村　晶**：1) Dicentric についていうと，20歳代で25%の細胞が fragment をもっていなかった．30歳代以上では観察された細胞はすべて X_1 であった．

2) 有意に高いということはなかった．

7. **Masuko TAGAWA, Naoki SADAMORI, Masako MATSUNAGA, Yu TOMONAGA, Miyuki KUSANO, Michito ICHIMARU** (Dept. Int. Med., Atomic Bomb Inst., Nagasaki Univ., Nagasaki) **Shotaro NERIISHI and Takeo HONDA** (RERF, Nagasaki): **Cytogenetic Observation of Bone Marrow in Acute Leukemia.**

Twenty three cases with acute leukemia were examined with Q and G banding method. The cases were 13 acute myelogeneous leukemia (AML), 5 smoldering leukemia (SL), 3 acute promyelocytic leukemia (APL), and 2 acute erythroleukemia

(EL). Diagnosis were established by clinical findings, smears and cytochemical method. Chromosome study was performed at initial stage of the course of illness before giving therapy. In each case, examination of over 20 metaphases including at least 3 karyotypes using Q and G banding method was done. A clone was defined to have more than 3 identical abnormal karyotypes.

The results: Of 23 cases, 10 cases showed normal karyotypes, and 13 showed clone with abnormal karyotypes as follows: Case 1 (52y/o, M, AML), 47, XY, +1, 5q−, 6p−., Case 2 (28y/o, M, AML), 46, XY, t(16p− ; 21q+)., Case 3 (20y/o, M, AML), 46, XY, t(6p+ ; 9q−), t(8q− ; 11p+)., Case 4 (56y/o, M, AML), 45, XO, t(8q− ; 21q+)., Case 5 (54y/o, M, AML), 45, XY, −21, t(2q− ; 11q+)., Case 6 (67y/o, M, AML), 41, −X, −Y, −13, −17, −20, −22, +M, 14q+., Case 7 (16y/o, M, AML), 36, XY, −2, −3, −4, −7, −12, −13, −16, −18, −19, −21 etc., Case 8 (59y/o, F, SL), 47, XX, +8., Case 9 (65y/o, M, SL), 47, XX, +8., Case 10 (66y/o, M, SL), 47, XYY, 20q−., Case 11 (88y/o, M, SL), 46, XY, 7q−., Case 12 (2y/o, M, EL), 49, XY, +6, +21, +21, 1q−., Case 13 (67y/o, M, EL), multiple change containing 45, XY, t(2p+ ; 5q−).

57% of total cases showed chromosomal aberration. Chromosome No. 2, 6, 8 and 21 seemed to have been involved mostly in non ramdom change of chromosome in acute leukemia. The cases which mediated far from normal modality appeared to have shown rather poor clinical course. (XYY in case 10 was constitutional change.)

8. **Nanao KAMADA, Nobuo OGUMA and Ryuji TANAKA** (Dept. Internal Med., Hiroshima Univ., Hiroshima): **Cytogenetic Studies of 110 Cases with Chronic Granulocytic Leukemia.**

During April 1962-October 1976, a total of 110, 64 male and 46 female, patients with chronic granulocytic leukemia (CGL) were seen in our Department. Ages at the time of diagnosis were ranged from 17 to 87 years old. Of the 110 patients 31 were directly exposed to the atomic bomb in 1945 and 10 were early entrants who entered to Hiroshima City within 3 days after the explosion. Five patients were sons or daughters (F_1) of the exposed parents. Chromosome aberrations in chronic phase: All but one patients had Philadelphia chromosome. Three patients had chromosome abnormalities other than Ph^1, showing 45, X, −Y, Ph^1, 45, X, −Y, Ph^1 and 46, XY, −C, Cq−, +mar, Ph^1.

Chromosome aberrations in blastic phase: Fifty two patients transformed to blastic phase, of which 33 were cytogenetically examined. Their karyotypes showed 4 hypo-diploidy, 11 normal diploidy, 5 pseudo-diploidy and 13 hyper-diploidy, represent-

ing 67% of chromosome aberrations in the 33 patients. Double Ph^1 chromosomes were found in 12 patients. E17 abnormalities, including isochromosome of E17, were observed in 8 patients. The 33 patients were categorized into three groups from the clinical features; acute form—an abruptive onset of blastic crisis accompanied by a high percentage of myeloblasts in the peripheral blood and a rapid enlargement of the spleen, transitional form—a gradual increase of myeloblasts without apparent Hiatus leukemicus, basophilia in the peripheral blood, retension of splenomegaly resulting from resistency to busulfan, and localized form—a preceding subjective symptoms such as bone or joint pain without any apparent hematological changes and a final development of myeloblastoma in the bones or lymphonodes. Cytogenetic studies on these three groups of patients revealed a high incidence of double Ph^1 chromosomes in the transitional form (6/14) and the localized form (4/7) and a high incidence of E17 abnormalities in the transitional form (7/14). Cases in the acute form had a tendency of hypo- or normal diploid karyotypes. On the other hand patients in the transitional form had pseudo- or hyper-diploid karyotypes. The tendency of hyper-diploidy was more predominantly observed in the localized form of blastic crisis.

It can be concluded that 1), Philadelphia negative CGL patients seemed to be very rare in Japan, 2), patients with abnormal karyotypes were thought to be less than 5 percent of the patients in chronic phase and 3), as chromosome abnormalities in blastic phase, double Ph^1 and E17 chromosome abnormalities were rather common, especially in the transitional form and the localized form of blastic crisis.

〔**質問**〕 **貞森直樹**（長崎大学・原研内科）：1) 症例中，初診時すでに急性転化をおこしていた例の臨床経過は．

2) 慢性期に clonal evolution がみつかり，その後長期に急性転化をおこさなかった例はなかったか．

〔**答**〕 **鎌田七男**：1) 初診時に急性期を呈したものは3例ある．1例は19歳女，強力な白血病治療により10カ月生存した．2例目は56歳男，2カ月で死亡．3例目は29歳女，2カ月現在治療中．

2) 慢性期から Ph^1 以外の異常を示し半年後に急性転化した例がある．今回の3例はいわゆるCML細胞の clonal evolution としての異常とは考えていない．

9. **Hiroko FUJITA, Yōko YOSHIDA** (Dept. Science Living, Univ. Osaka City), **Yōko TANIGAWA** (Lab. Tsukaguchi Hosp., Hyogo) **and Keiko TSUDA** (Lab. Aizenbashi Hosp., Osaka): **G and C-banding Pattern of Eight i(Xq) Cases and One X/X Translocation Case with Turner's Syndrome.**

This paper presents so cold iso-X chromosome of eight women with short stature and primary amenorrhea and of a 6-year-old girl with short stature. We, using the G and C banding methods, identified these 9 cases with iso-X chromosome as

three different types of iso-X and one X-X translocation as follows.

1) 46, X, i(Xq) (qter→cent→qter) for 4 cases. Both arms of the i(Xq) should a mirror-image of the X long arm in G-band pattern. The i(Xq)s should have been produced by transverse breakage of the centromere.

2) 46, X, i(Xq) (qter→p11→qter) for one case. This i(Xq) was similar to No. 2 chromosome in size and shape. G-band patterns disclosed q11 band on one arm being longer than that on the other arm. There were two C-bands on the i(Xq). One of them indicates a morphologically normal centromere but the other one is displaced at a proximal region of longer arm. From the above findings we suggest this i(Xq) might be produced by a single break at p11 of normal X and duplication of proximal short arm and complete long arm.

3) 45, X/46, X, i(Xq) (qter→p11:: p11→qter) for 3 cases. Both arms of i(Xq) showed asymmetric G-banding pattern because of having longer q11 band in one arm than that in other arm. C-banding, examined in two cases, demonstrated two centromeric bands in close position. In this case of mosaic type, i(Xq) formation should have occurred during mitosis of zygote. Perhaps, after chromatid doubling in late S or G_2, a break and a reunion occurred at the same position of two short arms on nonsister chromatids. As a result of it, a fragment and double chromatid consisting of qter to p11 which is i(Xq) chromosome are produced. After all, it is suggested that one daughter cell has only one normal X chromosome and another cell has one normal X and the i(Xq).

4) 45, X/46, X, t(X : X) (qter→p22:: p11→qter) for one case. This abnormal submetacentric chromosome, same as No. 1 chromosome in size, is identified as a translocation chromosome. With G-banding the break points are identified as p22 of one X chromosome and p11 of the other X chromosome. With C-banding two heterochromatins were detected. One is at centromere position and the other at the middle of longer arm. Concerning of mosaicism of this case, it is suggested that non-didjunction occurred and both XO and XXX daughter cells were yielded after formation of normal zygote. Then, X-X translocation occurred in the 47, XXX cell line.

10. **Hirofumi NAKAJIMA, Takeo HASIMOTO** (Dep. Neonat., St. Mary's Hosp., Kurume), **Shigeru TAKEYA** (Dep. Pediat., St. Mary's Hosp., Kurume), **Masato MARUYAMA** (Lab., St. Mary's Hosp., Kurume) **and Yasuo NAKAGOME** (Nat. Inst. Genet., Mishima): **4-p Trisomy.**

The trisomy of short arm of chromosome 4 appears to be a very rare condition, especially in Japan. The patient was a product of non-consanguineous and full-term delivery with the birth weight of 2,550 g. He was referred to St. Mary's

Hospital Neonatal Center because of cervical mass and abnormal external genitalia. The patient was delivered spontaneously with premature rupture of membrane. This boy was the first baby of the parents who had no history of abortion and were non-consanguineous. Family history was negative for abortion, still-birth or congenital malformation. When the patient was admitted, his face was distinctive with a stubby nose, depressed and broad nasal bridge, thin lip and elongated philtrum. He had broadening of the concha and helix of the ear; short neck and abnormal mass contained with abnormal cervical process; widely spaced nipple; small penis; cryptorchidism; abnormalities at the proximal area of the toe. The general condition was, however, relatively good until ten days after birth. At ten days of age, systolic murmur was audible and cyanosis was noticed at crying and feeding. Truncus arteriosus was diagnosed by right heart catheterization. At the age of one year, he showed severe psychomotor retardation and marked cyanosis. He had been observed in the incubator with oxygen. An X-ray examination showed scoliosis and eleven pairs of ribs; cardiac enlargement; left kidney was obscure by intravenous pyelogram. The computed tomography showed calcification on the cerebrum and slightly enlarged third ventricle. The electroencephalogram revealed a lazy pattern in the right and spike in the occipital and temporal area. Dermatographic study showed a predominance of whorl patterns on the finger.

Cytogenetic studies by trypsin-Giemsa banding method showed 46, XY, der(13), rcp(4; 13) (p12 or 13; p11) mat and diagnosed as 4-p Trisomy. His mother was confirmed as a carrier because she had karyotype of 46, XX, rcp(4; 13) (p12 or 13; p11). If compared with previous reports, truncus arteriosus and cervical mass were peculiar in this case.

11. **Kouzi NARAHARA, Hiroshi YABUUCHI, Shunsuke KIMURA and Hiroshi KIMOTO** (Dept. Pediat., Okayama Univ., Okayama): **A Case of Nonmongoloid Trisomy G (47, XX, +del(X) (p22q13)).**

A case of nonmongoloid trisomy G studied by G-, Q-, R- and C-bandings is presented. The patient, a 18-month-old female, was born at term to a 26-year-old, gravida 2, para 2, mother and a 28-year-old father. The birthweight was 2,730 g. Her brother was normal. At the age of three months congenital dislocation of the right hip joint was treated. She showed delayed psychomotor development, flat nasal bridge, downward slanted palpebral fissures, muscular hypotonia and stereotypic movements of the hands. Abnormal laboratory findings were increased serum creatine phosphokinase (203 mU/ml) and decreased leucocyte alkaline phosphatase (13%). There were no specific findings in dermatoglyphic study. Exami-

nation of the buccal smear showed X-chromatin found in a normal percentage of cells (23.5%), one in number and normal in size. Chromosome analysis of peripheral blood revealed an additional nonsatellited small acrocentric chromosome similar to those of group G in all cells. Based on the results of G-, Q-, R- and C-bandings, the extra chromosome was considered to be a centric fragment of X chromosome. The karyotype was therefore 47, XX, +del(X) (p22q13). Her parents and brother had normal G-banding karyotype. The lack of distinctive features in this case might be due to the fact that the extra chromosome was a part of X chromosome.

〔**質問**〕 **山本佳史**（神奈川こども医療センター）：1) Xの短腕のバンドまでの距離と，過剰染色体長腕のバンドまでの距離とが常に異なるように思うが如何.

2) X短腕の部分トリソミーとすると，表現型との相関はどのように考えるか.

〔**答**〕 **檜原幸二**：1) 過剰染色体とX染色体との G-band の距離が多少異なるようにみえるが，G-band pattern と臨床症状から他の染色体由来とは考えられず，X染色体と同定した.

2) Triplo-X には表現型の異常が少ないのと同様と考える.

〔**質問**〕 **近藤郁子**（筑波大）：この症例の場合，性染色質検査よりみて，過剰X染色体の遺伝的不活性化についてどのように考えられるか.

〔**答**〕 **檜原幸二**：性染色質形成の場はX染色体長腕と考えられている.

12. **Hiroshi NAKAI, Yoshifumi YAMAMOTO and Yoshikazu KUROKI** (Div. Med. Genet., Kanagawa Children's Medical Center, Kanagawa): **Inherited Pericentric Inversion of Y Chromosome in a Patient with Trisomic Down's Syndrome. The First Case in Japanese.**

Five cases with pericentric inversion Y and Down's syndrome, 47, X, inv(Y), +21, have been reported (Berger *et al.*, 1970; Baheux *et al.*, 1970; Sparkes *et al.*, 1970; Orye, 1974 and Sagredo *et al.*, 1975). We report the first case in Japan, and studied the incidence of pericentric inversion of Y chromosome in Japanese male population. We also tried to determine the origin of the extra chromosome 21, but not successful.

The propositus was born on September 19th, 1975 after 37 weeks gestation as the first product of normal parents with no consanguinity. His birth weight was 2,490 g. Physical and psychomotor developement was slightly retarded and he had typical features of Down's syndrome. The presence of inv(Y) gave no distortion on the clinical features. The karyotype of blood lymphocytes from the proband was 47, X, inv(Y), +21. The abnormal Y chromosome was intensively fluorescent on its one arm so that it was interpreted as a pericentric inversion Y. The mother's karyotype was normal but the father's showed an inverted Y.

In the newborn surveys, the prevalence of pericentric inv(Y) in general male population was suggested to be one or two per 1,000 (Walzer *et al.*, 1969; Gerald

and Walzer, 1970; Friedrich and Nielson, 1974). In our study, we sent questionaires to several laboratries in Japan in order to clarify the incidence of inv(Y). From the total number of about 5,000 males two such cases were detected (0.04%). Though there were some biases of ascertainment in this survey, we may conclude that the incidence is slightly lower in Japan. If there is a meaningful relation between the occurrence of inv(Y) and trisomy 21, it would be necessary to show that the extra 21 had originated from the father. Therefore, we tried to determine the origin of the chromosome 21, but any identifiable polymorphism could not be found and failed to decide the origin.

13. **Toshihiro OKAMURA,** (Yuri Nokyo Gen. Hosp., Akita): **A Case of Probable Trisomy 22.**

Case: Y.S. He was born 14th July, 1975. At the time of birth of this male child, the father was 28 years of age, and the mother was 21 years and gravida 1, para 1, abortus 0. Birth weight was 2,100 g in a 41 weeks gestation. The family history showed nothing to be mentioned and no consanguinity. Physical examination revealed: a characteristic face with long cellia, microcephaly, slight low set ears, high arched palate with blue pigmentation, abnormal pale ocular disc, short neck and rs. torticollis, inguinal hernias, retentio testis, and hypotonic muscles. He showed severe mental retardation and delayed development. ECG and radiographs showed congenital heart desease (V.S.D.). In Addition, radiographs confirmed the presence of bilateral congenitally dislocated hips. The peripheral leukocyte cultures of the patient revealed 47 chromosomes with an extra small acrocentric chromosome, which was identical in appearance to a G-group chromosome. Q and G-banding were applied for peripheral leukocyte cultures. The extra small acrocentric chromosome was identified as No. 22. Trisomy 22 syndrome presents less remarkable physical abnormalites. I think that clinical features, mental retardation, delayed development, doll like face, hypotonia, congenital heart desease and bilateral luxatio congenita coxae are characteristic for Trisomy 22.

〔追加〕 **黒木良和** (神奈川こどもセンター): われわれも1例経験した (昨年の本学会で報告) が, 阿波おどり様の特有な異常運動がみられた. この症状が将来出てくるか興味あるところと思う.

14. **Akiko URANO and Akira TONOMURA** (Dept. Cytogenetics, MRI, Tokyo Med. Dent. Univ., Tokyo): **The Origin of the Extra Chromosome No. 21 in Down's Syndrome.**

In order to clarify the origin of the extra chromosome No. 21 in Down's syndrome, we have analysed the 3 chromosomes No. 21 in the patients and in the parents,

using the quinacrine fluorescence technique. The informations concerning the origin of the extra No. 21 were obtained in 5 out of 14 cases examined.

In the first case, the satellites of both the chromosomes No. 21 were not clear in the father, while those were clearly identified in the mother. The patient had two No. 21s with satellites and one without visible satellites. The extra No. 21 was maternal origin, indicating the result of nondisjunction either in the 1st or 2nd meiotic division. In the second case, one of the two No. 21s had satellites with fluorescence and the other did not show visible satellites in the mother. The father had large satellites in one of the two chromosomes No. 21. The patient received two No. 21s with satellites and one with no visible satellites. There was no large satellites in the 3 chromosomes No. 21. The extra No. 21 was maternal origin, obviously the result of nondisjunction in the 2nd meiotic division. Based on the satellites and/or short arms with or without visible fluorescence, the extra No. 21 of the third case was identified as the paternal origin, in which nondisjunction occurred in the 2nd division. In the 4th and 5th cases, the extra chromosomes were maternal origin in both and derived from the result of nondisjunction in the 1st meiotic division. The paternal and maternal ages at the birth of the patients were 31 and 26, 30 and 28, 33 and 32, 30 and 28 and 31 and 23 years old in the 1st, 2nd, 3rd, 4th and 5th cases respectively.

Adding our data to the reported cases in Japan, there are 27 cases of Down's syndrome in which the origin of the extra chromosome No. 21 was traced.

〔質問〕 **大浜紘三**(広島大・産婦人科)：母体年齢の上昇と母親由来過剰21染色体を示す例との間に関連性が認められるか.

〔答〕 **浦野明子**：症例数が少ないために，関連の有無については不明である.

〔質問〕 **遠藤 晃**(山形大)：母親由来の場合，ＭＩとＭII別にみて平均母分娩年齢は如何.

〔答〕 **浦野明子**：ＭＩは 27.4 歳，ＭII は 28.3 歳であった.

15. **Fumiko SAITO and Akira TONOMURA** (Dept. Cytogenet., Tokyo Med. and Dent. Univ., Tokyo): **Chromosome Aberrations in Cultured Lymphocytes of Patients with Trisomy 21.**

Cultured lymphocytes of patients with Down's syndrome (D.S.) have been noted to have an increased chromosomal sensitivities to ionizing radiations or viral infections. In the present study, we have examined the frequencies and types of chromosome aberrations spontaneously occurring in D.S. patients.

Chromosome preparations were made by means of 48-hr lymphocyte cultures from 200 D.S. patients (mean age 1.9 yrs) and from 3 mosaic patients with 46, XX or XY/47, XX or XY, +21 (mean age 0.7 yrs). Most of the patients here examined, however, have had X-ray examinations for diagnosis several times. Therefore,

the results of the exposed and unexposed patients were compared with those of 9 in-utero exposed and 10 unexposed normal newborns respectively.

In the two exposed groups the frequencies of chromosome-type aberrations were 0.58% in the D.S. patients and 0.23% in the control, and those of chromatid-type aberrations (except gaps and iso-gaps) were 2.31% in the D.S. patients and 0.58% in the control. The frequencies of both type aberrations in the D.S. patients were significantly greater than those in the control ($p<0.05$ for chromosome-type, $p<0.001$ for chromatid-type). In two unexposed groups, the frequency of chromosome-type aberrations in the D.S. patients (0.33%) was higher than that in the control (0.18%) but the difference between the two groups was not significant. On the other hand, the frequencies of chromatid-type aberrations were 3.67% in the D.S. patients and 0.95% in the control. There was a significant difference between the two groups ($p<0.001$).

In the three mosaic D.S. patients (one was unexposed and two were exposed), the frequencies of chromosome-type aberrations in the trisomic cells were 0.56, 0.64 and 0.93%, and in the normal cells 0.00, 0.18 and 0.24% respectively, while the frequencies of chromatid-type aberrations were 1.69, 1.92 and 4.29% in the trisomic cells and those were 1.28, 1.45 and 3.42% in the normal cells. The frequencies of both types of aberrations were higher in the trisomic cells than in the normal cells in each of three subjects only the difference of chromosome-type aberrations was statistically significant in one of the two exposed mosaics. No significant difference of the levels of chromatid-type aberrations between trisomic and normal cells in the mosaics was not parallel with the results obtained from the comparison of trisomic cells of D.S. patients and cells of newborns with anormal karyotype. This might due to the difference of culture conditions or different persons with different backgrounds.

〔**質問**〕 **阿波章夫**（放影研，広島）：ダウン症児は正常に比べてX線照射の機会が多いとのことだが，線量との関連性が重要な要因と考えられるので，具体的にどの程度（照射部位等）被曝しているか伺いたい．

〔**答**〕 **外村　晶**：主に国立国府台病院の患児が対象で，股関節，胸部，全身等のレントゲン撮影を数回から10回ほど受けている．

16. **Ryuichi TSUKINO, Michio KOIKE, Hiromi SAKAI, Toyokazu MORIHATA and Teisuke KODAMA** (Dept. Pediat., Wakayama Med. Col., Wakayama): **A Case of Ring Chromosome 10.—A New Autosomal Deletion Syndrome.**

K.J., a 1 1/2-year-old girl was born 6/26/'75 to a 23-year-old gravida 1, para 1 mother. The patient was developmentally retarded: mild stubby nose, erythrocyanosis and edema in both hands and feet, pigmentation as was seen in *Inconti-*

nentia Pigmenti in lower extremities, high position of axial triradius and so on. Parents were Japanese, unlelated, healthy and of normal height and intelligence. At 3 month of gestation, her mother had the sign of threatened spontaneous abortion and was injected 5 times weekly. After 42 weeks of uncomplicated gestation, the patient was delivered spontaneously from occipitoposterior position. Birth weight was 2,500 g. The newborn was entirely normal but her feeding was poor. At 6 months, she was sent to our hospital with chief complaints of retarded growth. Developmental milestones were mildly delayed. She held her head at 8 months and walked with support at 12 months. She can speak few wards now (18 months).

Laboratory and physical examinations including EEG, brain echography, radiography of chest, skull and hands, routine blood examinations, liver functions, thyroid functions, and metabolic screening tests on urine were all within normal range. There were many atrophic areas in both chorioides. IVP showed non-obstructive dilatation of right pelvis and calyces.

Chromosome studies performed with standard banding techniques (G and C-bandings) and autoradiography showed 46, XX, r(10) (p13—q26). By routine chromosome analysis of 72 hr culture, there were three cell populations (chromosome numbers 45 without ring, 46 with normal size ring, 47 with 2 rings, and 46 with a large ring). The large ring chromosome had twice the normal ring chromosome size with 2 centromeres by C-band. The origin of these abnormal chromosome was examined by changing incubation time 48-168 hr.

17. **野本直記・立神恭之**（京都市立病院・小児科）：**10 番染色体長腕の部分的トリソミーの剖検例**. Naoki NOMOTO and Yasuyuki TATUGAMI (Kyoto City Hosp., Kyoto): **Partial Trisomy for the Distal Two-Third of the Long Arm of Chromosome 10 due to Duplication.**

妊娠42週で出生．生下時体重 1,640 g，身長 38.5 cm，頭囲 29.5 cm，胸囲 27.6 cm．母 27 歳，父 31 歳．第2子で両親長女とも健康．近親婚なし．呼吸器系および循環器系異常が著明で生後間もなく保育器に収容した．また尿所見で血尿がみられ，腎奇形も疑われた．生後 42 日目に心不全，腎不全の状態で死亡した．主な奇形を列記する．小頭症，広い額，扁平かつ円い顔．弓状で広い眉毛，眼裂縮少，眼裂の下方傾斜，眼瞼下垂，右眼のみの小眼球症，白内障，下方の虹彩欠損．小さな鼻，扁平鼻橋，弓状の小さな口，口蓋裂，舌繋帯過長症，小顎症．低位耳介付着，変形した耳．短頚．鳩胸．屈指症，第 2,3,4 指の単一屈曲線，猿線．剖検により，interruption of aortic arch Type II，多嚢胞腎（Type III by Osathanondh and Potter），右肺の分葉異常を主所見とした．末梢リンパ球染色体検査でのGバンドおよび症例検討により，10番染色体長腕の部分的トリソミーと診断した．これは成熟分裂での intrachromosomal duplication によるものであろう．両親長女ともに正常核型であった．

18. **Noriho TANAKA** (Dept. Hygiene, Kagoshima Univ., Kagoshima), **Tatsuro IKEUCHI** (Chromosome Res. Unit. Hokkaido Univ., Sapporo), **Keida KITAHARA, Isao YARA and Taku NAGAI** (Kagoshima Univ., Kagoshima):
A Case of Trisomy 9p Deriving from Maternal Complex Translocation.

The patient was born at 40 weeks after uneventiful pregnancy, weighing 2,700 g. She was standing at 20 weeks and walked at 2 years. At the age of 9 years, she was admitted to an institution for mentally retarded children, and thereafter she received an operation for patent ductus arteriosus with pulmonary hypertension.

On examination at 10 5/12 years of age, height was 106.5 cm (the standard value, 135.5 cm); weight, 17.0 kg (29.98 kg); head circumference, 48.0 cm (52.2 cm); and chest circumference, 62.0 cm (64.3 cm). Her mental age was given as 2 2/12 years on the Suzuki-Binet intelligence scale (I.Q., 21). Clinical examination showed multiple congenital anomalies: hypertelorism with a slight antimongoloid slant, short neck, flat nose, high hard palate, funnel chest, heart malformation, odontoloxia and kyphoscoliosis. In extremities, there were noted the short fifth fingers with hypoplastic nails, only one flexion crease on the 2nd, 3rd and 5th fingers on both hands, and hypoplastic nails on the fifth toes. X-ray examination revealed kyphoscoliosis with multiple bone defects. Blood counts, serum immunoglobin levels of IgG, IgA and IgM were within normal range. Steroid hormones of 17-KS (0.9 mg/24 hr) and 17-OHCS (1.1 mg/24 hr) showed a low level as compared with normal values (17-KS, 7-20 mg/24 hr; 17-OHCS, 6-20 mg/hr). Other laboratory findings, alkaline and acid phosphatases, total cholesterol, creatine, LDH, GPT and GOT were all normal. No anomalies were found in the segregation of the following genetic markers: serum heptoglobin and blood types of ABO, MNS and Rh. Dermatoglyphic analysis showed an excess of arches in digital patterns with a low total ridge count of 34. The axial triradii were in the normal position. No simian crease was found.

The result of chromosome analysis of the patient showed a partial trisomy of 9p deriving from her mother. Based on G and Q-banding patterns, the karyotype phenotypically normal mother was 46, XX, t(4; 6; 9) (4pter→4q3:: 6p1→6pter; 6qter→6p1:: 9p1→9pter; 9qter→9q1:: 4q3→4qter). The karyotype of the patient is therefore 46, XX, −4, −6, +t(4; 6) (4pter→4q3:: 6p1→6pter), +t(6; 9) (6pter→6p1:: 9p1→9pter) mat. Examination of leucocytes cultures from the her brother, father, grandmother and grandfather revealed normal karyotypes.

〔**質問**〕 **藤田弘子**（大阪市大・生活科学）：1) 骨年齢遅延はみられなかったか.

2) 成長ホルモンの検査は如何. 貴症例に侏儒症があるようだが，成長ホルモンの検査が行われていたら教えてほしい. 私の 3〜6 歳の 3 症例の経験では，成長ホルモン欠損（おそらく視床下部→下垂体系の異常）が認められている. しかし，15歳の症例では骨発達の著明な遅れがあるにもかかわらず

成長ホルモンは正常範囲であった.

〔答〕 **田中憲穂**：1) 骨年齢の低下はみられた.

2) 成長ホルモンは測定していない.

〔質問〕 **柳沢 慧**（山口大・小児）：No. 9 の break point は如何.

〔答〕 **田中憲穂**：P13 であることが推定される.

19. **宮崎玲子・百井 亨・谷岡賢一・須藤克己**（京大・小児科）・**阿部達生**（京府医大・公衆衛生）：**表現型に多彩な異常を認めた Pericentric Inversion の一例**. Reiko MIYAZAKI, Toru MOMOI, Kenichi TANIOKA, Katsumi SUDO (Dept. Pediat., Kyoto Univ. Med., Kyoto) and Tatsuo ABE (Dept. Public Health, Kyoto Prefect. Univ., Kyoto): **Pericentric Inversion of Chromosome 9 Found in a Girl with Multiple Malformations.**

最近，Qあるいは C-band を用いる多形解析によって，正常な新生児の中に pericentric inversion を示すものが，かなり発見されている．また pericentric inversion は satellite DNA の逆転に限られることが多いので，一般に臨床症状を呈することが少ないと言われている．われわれは，発育遅延，多発奇形を示した4カ月の女児の染色体分析にて，中部着糸型の pericentric inversion を示す染色体を認めた．さらに両親の検索を進めたところ，表現型に異常を認めない父親に，発端者と同様な pericentric inversion を認め，正確に transmit されていることがわかった．発端者に見られた様々な表現型の異常を，pericentric inversion に求めながら，両親の検索によって，これが否定された一例を経験したので報告した.

20. **Hiroko AOKI, Akira TONOMURA** (Dept. Cytogenet., Tokyo Med. Dent. Univ., Tokyo), **Mitsushiro KIDA** (Dept. Pediat., Teikyo Univ., Tokyo) **and Tatsuo NAITO** (Dept. Neonat., Nat. Child. Hosp., Tokyo): **Chromosome Analysis in the Progeny of t(7;9) (q22;p24) Translocation Carriers.**

The estimation of the segregation ratio between the balanced translocation and the normal complement in the progeny of translocation carriers is an important problem both in human population cytogenetics and in practice of genetic counseling. Recently, we have had an opportunity to examine a case of reciprocal translocation between the long arm of chromosome No. 7 and the short arm of chromosome No. 9 in a family and it's relatives. The propositus was a 3-months-old boy with brachycephaly, antimongoloid slant, exophthalmus, prominent nasal bridge, micrognathia, high arched palate, low set and malformed ear, rocker bottom foot, joint limitation and inability to fully extent of limbs, hypertonia, short stature and developmental retardation. He showed an unbalanced karyotype and the mother had a balanced reciprocal translocation. Using the ASG staining technique, it was identified that the reciprocal translocation has occurred at band 7q22 in the long arm and band 9p24 in the short arm of chromosomes Nos. 7 and 9, respectively. The karyotype of the propositus was thus designated as 46, XY, der(9), t(7; 9) (q22; p24) mat.

After the examination of chromosomes in relative persons of the mother, 10 of

16 relatives were found to be the translocation carrier. The ratio of normal karyotypes to translocation carriers was somewhat different from the expected 1 : 1 ratio in the progeny of carrier parents ($0.01<p<0.02$). This may suggest that small selective advantage in the balanced translocations can not be excluded in the present instance.

There are a number of spontaneous abortions and an early death during the first year after the birth, and a cousin of the propositus who died at 2 months after the birth had multiple congenital abnormalities. If these cases are taken into account, the maximum risk of affected children was estimated as 0.25 in the present case. This value is comparable to the estimation risk (0.26) by Lejeune (1970).

21. **本田幸子・林美貴子・渡辺正男**（富山衛研）・**福井　悟**（福井病院）・**松田健史**（富医薬大・解剖）：**母娘にみられた 9/21 の転座型保因者の一家系について.** Sachiko HONDA, Mikiko HAYASHI, Masao WATANABE (Toyama Inst. Health., Toyama), Satoru FUKUI (Fukui Hosp., Tonami), and Takeshi MATSUDA (Dept. Anat., Toyama Med. Pharm. Univ., Toyama): **Karyotype-analysis of a Pedigree, in which 9/21 Balanced Translocation was Observed on the Propositus and Her Daughter.**

精神病患者3人を有し，9/21転座型染色体を2代にわたり保因する一家系の染色体検査を行い，精神病と染色体異常の有無，切断点についての考察を行った.

発端者（34歳女），その叔父（死亡）と妹（26歳）が発病しており，発端者とその娘（10歳）が転座型保因者であった．発端者の妹，父，母と叔母は染色体的には正常であった．また，発端者の妊娠中，異常はなかった．精神病3人のうち，1人のみが転座型保因者であったこと等から，精神病と9/21 転座型染色体保因との関係は確認しえなかった．また，G. Q. C-バンド法等により，No. 9 と No. 21 の相互転座であり，切断点は 9q12 と 21q11 バンドであると考えられ，母娘の核型は同じく，46, XX, t(9; 21)(q12; q11)，46, XX, t(9; 21)(9pter→9q12:; 21q11→21qter; 21pter→21q11:; 9q12→9qter) であると決定した.

22. **Yoshikazu KUROKI, Shunpei YOKOTA, Hiroshi NAKAI, Yoshifumi YAMAMOTO and Ichiro MATSUI** (Div. Med. Genet., Kanagawa Child. Med. Cent., Yokohama): **A Case of 9p− Syndrome in Japan.**

A new case of 9p− syndrome from Japan is presented. As all reported cases were Caucasians, it is of importance to present the first case observed in Oriental.

KC-39139, a 8 month old female, was sent to Kanagawa children's medical center because of developmental retardation and of suspected Down's syndrome. She was the full-term product of a 28 year old mother and a 33 year old father after an uneventful course of pregnancy and normal delivery. The parents were healthy and non-consanguineous. The mother experienced 3 spontaneous abortions.

Her birth weight was 2,970 g, length was 51.5 cm, and head circumference was 32 cm. Her growth was almost normal. She could smile at 3 months of age, could control her head at the age of 5 months, but she could not sit alone or roll over. Her DQ was 50 at the age of 8 months. On physical examination, unusual facial features of round, poor-reliefed and dysmorphic impression were noted. The head was trigonocephalic with prominent forehead and flat occiput. No microcephaly was noted. There were small palpebular fissures, a mongoloid slant of the eyes, a flat and small nose with anteverted nostrils and long philtrum. The ears were set slightly low with prominent antihelix. The mouth was small with somewhat protruding lips. There was micrognathia and the neck was short with myogenic torticollis.

The examination of the thorax and abdomen revealed wide-set nipples, closing VSD and bilateral inguinal hernias. The spine showed mild scoliosis. The fingers and toes were long, due to increased length of the middle phalanges. The nails were square and hyperconvex. Mild flexion contracture was noted on the knee joints and there was clinodactyly on IV and V toes. Dermatoglyphics showed ten whorls on the fingers, and the total finger ridge count was 233. All of the laboratory examinations, including hematological examination, urynalysis, blood chemistry, endocrinological tests and electrophysiologic examinations, revealed normal. Pneumoencephalography showed mild diffuse ventricular enlargement and moderate cortical atrophy.

Chromosome examination was performed by use of peripheral leucocytes. Analysis of the G-banding was done both in the proband and parents. The karyotype of the proband revealed 46, XX, del(9) (qter→p22:). The parents had normal karyotypes.

Most of the clinical features in the present case were very similar to those of Caucasian cases in the literature. This suggests the presence of a well identifyable clinical entity associated with the 9p− karyotype.

23. **上原真理子・木田盈四郎・松原富子** (帝京大・小児科): **10p− の一例.** Mariko UEHARA, Mitsushiro KIDA, Tomiko MATSUBARA (Dept. Pediat., Univ. Teikyo, Tokyo): **A Case of 10p−.**

10p−の1自験例に加えて，文献例の10p−(2例)，10p+(5例)，10p−を含む転座型(2例)の染色体異常のかたちと臨床症状について比較検討したので報告する．

自験例は8歳女児で主な臨床症状は，精神発達遅延，筋低緊張，短頭，鼻背低下，両眼間隔離，小眼球，高口蓋，巨舌，耳介低位，外反肘，長い手掌および紡錘状手指，内反足等である．G banding法による染色体分析の結果は，46, XX, del (10) (p13) であった．なお両親の染色体に異常は認められなかった．

一方，文献例の核型には del(10) (p13)—(男1女2)，der(7) (7：10) (p22：p11)—(姉弟)，der(7) (7：10) (q35：p14)—(男)，der(22)，t(10：22) (p11：p11)—(同一母からの流産胎児：男女) および inv(4) (p16q21)t(inv(4)：10) (q35：p14)t(13q14q)—(女)，der(10)t(10：14) (p15：q13)—(男) が見られた．

次に42の臨床症状について 10p+，10p− の頻度を求めた結果，高いものだけをとると，眼裂斜下，鼻背低下，短頭，耳介前くぼみ，乳頭間隔離，紡錘状手指，細長い手掌，胸郭変形は 10p− のみに，眼裂斜上，鼻背隆起，長頭は 10p+ のみにみられる．また高口蓋は 10p− で，兎唇口蓋裂，性器異常，筋低緊張，前頭隆起，高い前頭は 10p+ で比較的高い頻度で現れ，下肢変形，精神発達遅延，耳介低位は両者に共通に高い頻度であらわれている．全体の傾向としては，10p− では症状の軽いものが多くみられ，また頻度の低いもの，特有なものが多いのに対して，10p+ では逆の傾向がみられた．一方，10p− を含む転座型の臨床像は 10p− と近い傾向にあることがわかった．

24. **木田盈四郎・上原真理子**（帝京大・小児科）：**18環状染色体の一症例および18部分的モノソミーの臨床症状の意味について．** Mitsushiro KIDA, Mariko UEHARA (Dept. Pediat., Teikyo Univ., Tokyo): **A Case of 18 Ring Chromosome and Clinical Significance of 18 Partial Monosomy.**

患者は3歳3カ月の男児で，染色体検査の結果18番染色体が環状であることがわかった．両親の染色体は正常で，児は母親28歳，父親29歳の時生れている．IgG は 960，840 mg/dl，IgA は 94，61 mg/dl，IgM は 146，170 mg/dl とそれぞれ正常範囲であった．症状は，小頭症 (40.4 cm)，両眼隔離，内眼角ぜい皮，鼻背低下，鼻翼低形成，小顎，高口蓋，魚状の口，耳介異形成，難聴，紡錘状の指，猿線，II-III 趾間の皮膚性合趾症，関節過伸展，筋低緊張，潜伏睾丸，陰茎異形成，先天性心奇形，肝腫，低身長 (69.4 cm)，精神運動発達遅延，顔面中央部後退などがみられた．

文献上 18p− の 44例，18q− の 29例，18r の 39例を集めて，その臨床症状について検討した．記載されている27症状について，それぞれの出現頻度を調査した．その結果を比較検討する場合に問題となるのは，文献に記載されていないものの取扱いである．記載されていないものを陰性とみなす (Kunze, 1972) 立場もあれば，除外して考える (Lurie, 1972) 立場もある．両者とも正しいと思えぬものがある．そこで，その平均値をとった．18p− と 18q− の両群についてその比（尤度比）を計算した．その値が 0.5 以下のものは 18q− の特徴を比較的強く現わすと考えられ，外耳道狭窄，聴力障害，眼振，紡錘状の指，運動発達遅延，先天性心疾患，渦状紋6指以上，外陰部奇形などが含まれ，その値が1.5以上のものには，小顎症，眼瞼下垂，翼状頚，斜視，内眼角ぜい皮，両眼隔離が含まれていた．これは 18q− の特徴が強いと考えられる．同時に，18r についても調べたが，その傾向は両者にまたがっていた．

25. **中野省三・服部愛子・西岡研哉・奥野武彦・北条博厚**（京大・小児科）・**阿部達生**（京府医大・公衛）：**比較的まれな染色体異常3例について—46, XY, 18p−, 46, XX, t(13；14), r(14), 45, X, t(22；X)mat.** Shozo NAKANO, Aiko HATTORI, Kenya NISHIOKA, Takehiko OKUNO, Hiroatsu HOJO (Dept. Pediat., Univ. Kyoto, Kyoto), **Tatsuo ABE** (Dept. Prev. Med., Kyoto Pref. Univ. Med., Kyoto)：**Three Cases with Rare Chromosome Anomalies—46, XY, 18p−, 46, XX, t(13；14), r(14) and 45, X, t(22；X)mat.**

症例 1.　11カ月の男児で，父39歳母32歳の第1子として生れた．在胎42週 2,069 g で生まれ，生

下時から哺乳力弱く，体重増加も不良であった．眼瞼下垂，眼球開離，眼内角贅皮を認め，耳介は大きく突出して低位付着を示し，小顎症，への字型の口唇，短頚，斜頚，小陰茎を認め，筋緊張は，やや低下していた．レントゲン写真にて，胸椎の hemivertebrae および肋骨の unsegmentation を認め，心陰影は，右胸位を示した．DQ 69 で，免疫グロブリンは正常であった．染色体検査にて 46, XY, del(18) (p1104) と判明した．両親では，異常は認めなかった．

症例 2. 2歳6カ月の女児で，父 28 歳母 24 歳の第1子として生れた．在胎40週 3,650 g で生まれ，6カ月頃から全身性間代性痙攣を繰り返した．体格は標準であったが，顔貌は表情に乏しく，antimongoloid slanting，眼球開離，耳介低位付着，皮膚粘膜の色素沈着および白斑を認め，眼底検査にて，網膜周辺部の黒色色素斑を認めた．気脳写にて脳室拡大，脳波では，高振幅徐波および鋭波を認めた．DQ41 であったが，運動面よりも，社会性，適応性の面での遅れが著明であった．染色体検査では，No. 13 と 14 の相互転座および No. 14 の ring 形成を認めた．すなわち，核型は 46, XX, t(13; 14) (p11; q24) r(14) (p13→q24) であった．両親では，異常は認めなかった．

症例 3. 1歳8カ月の女児で，母親は 28 歳であったが，流死産を6回経験していた．今回も性器出血のため，子宮口結紮術を受けた．患児は在胎 40 週で，帝切にて 2,722 g で出生したが，生直後からチアノーゼを認め，心雑音を指摘された．眉毛が濃く，鼻根部やや膨隆し眼瞼下垂，眼内角贅皮，耳介低位を認めた．筋緊張やや亢進し，心雑音聴取し，DQ47，脳波では徐波成分が多かった．染色体検査では発端者は No. 22 が欠失，母親は，Ph^1 に酷似した染色体を認めた．No. 22 の長腕の一部がX染色体に転座していることが判明した．すなわち，患児核型は 45, X, t(22; X) (q11; p12)$_{mat}$ である．末梢血液像，好中球 Alp には異常は認めなかった．

26. **Tatsuo ABE, Masuji MORITA** (Dept. of Preventive Med.), **Shinichi MISAWA** (Dept. of Med., Kyoto Pref. Univ. Med., Kyoto), **Taku HASHIMOTO** (Dept. of Pediat., Maizuru Natl. Hosp.) **and Yasuo NAKAGOME** (Dept. of Hum. Genet., Natl. Inst. Genet., Mishima): **Partial Tetrasomy of the Chromosome 9—Analysis of an Aberrant Chromosome by Various Bandings.**

A 3-year-old boy with partial tetrasomy of no. 9 chromosome is reported. The propositus, T.K., was born to a 35-year-old mother and 38-year-old father. Both parents and the only sister showed no abnormalities. At birth, the weight was 2,900 g. He gained poorly and his psychmotor development was markedly delayed. It was noticed that the infant was deaf. An evaluation of his development at the age of 19 months revealed a development quotient of 13. At 3 years of age, he was not able to control his head. Physical examinations revealed marked retardation of physical and psychomotor development, brachycephalia, open fontanel, hypertelorism, epicanthic folds, strabismus, wide bulbos nose, downward slant of the corners of the mouth, micrognathia, low-set and malformed ears, high-arched palate, hypoplastic scrotum, hypoplasia of distal phalanges, overlapped second finger onto the third, general muscle hypotonia, and deafness. Laboratory studies, including intravenous pyelography, were unremarkable. Dermatoglyphic studies disclosed simian lines, absence of c triradii and low axial triradii, on both palms.

Digital patterns were UWUWU and AWUWU for right and left hands, respectively.

Routine chromosome analysis revealed an extra C-group chromosome. It had a pronounced secondary constriction at the proximal part of its long arm. Based on studies by a variety of banding techniques, the extra C chromosome was identified to be an iso-dicentric no. 9 chromosome with inactivation of one of the two centromeres, karyotype being 47, XY, +dic(9) (pter→q2101:: q2101→pter). The value of BudR treatment was emphasized in the detection of a small piece of euchromatin within a long stretch of constitutive heterochromatin. (The full paper will be published in the Ann. Génét.)

27. **Tatsuo ABE, Masuji MORITA, Shinichi MISAWA** (Dept. of Prev. Med., Kyoto Pref. Univ. Med., Kyoto), **and Hiroko CHISHIRO** (Dept. of Pediat., Ohmi-Hachiman Municipal, Hosp., Shiga): **Trisomy 9p Found in Two Sibs Resulting from Maternal Translocation.**

Trisomy 9p found in two sibs, aged 23 and 27 years, is reported. The both propositi were found to have following clinical features: mental retardation, short stature (propositus, 149 cm, proposita, 146 cm), big and bulbos nose, deep-set eye, hypertelorism, slight anti-mongoloid palpebral fissure, prominent ears, short neck, tapering fingers with webs, distally implanted big toes, and immatured genitals. Abnormal palm prints and simian crease were noticed on both hands of propositi. IQ was about 40 in both patients.

Conventional Giemsa staining showed that the extra chromosome had nearly same morphological appearance as the group G chromosomes. Both parents showed apparently normal chromosome constitution. Q-Banding analysis revealed, however, that the abnormal chromosome found in both propositi was del(9) (9pter→9q12). Therefore, they were found to be trisomic for the short arm of the chromosome 9. Transmission was from their mother, whose chromosome constitution could be described as 46, XX, t(9; 22), (9pter→9q12:: 22pter→22p13; 22qter→22p13:: 9qter→9q12). (The full paper will be published in this journal).

28. **Kunikazu KISHI and Akira TONOMURA** (Dept. Cytogenet., Tokyo Med. and Dent. Univ., Tokyo): **Analysis of Some Properties of Two Sub-Populations in Phytohemagglutinin (PHA)-Responding Lymphocytes: A Comparison of 21-Trisomic Cells and Normal Diploid Cells.**

Patients with Down's syndrome are different from normal persons not only in their mental and physical developments, but also in their chromosomal radiosensitivity and susceptibilities to leukemia or viruses. The aim of this study is to compare the following properties of PHA-responding lymphocytes between trisomic and

normal cells; the cell cycle times and durations of component phases, the proportions of two sub-populations at 72 hr after PHA stimulation and the chromosomal sensitivity to incorporated ^{3}H-thymidine (TdR).

The mean durations of post-DNA synthetic phase plus mitosis and of DNA synthetic phase in the trisomic cells were 3.8 hr and 7.4 hr, while those in the normal cells were 4.3 hr and 7.7 hr respectively. Since there were two distinct sub-populations in their cell cycles in PHA responding lymphocytes, the mean cell cycles and durations of pre-DNA synthetic phase of two sub-populations were compared in both trisomic and normal cells. The durations of pre-DNA synthetic phase in shorter and longer cell cycle sub-populations were 2.0 hr and 11.1 hr for trisomic cells and 0.1 hr and 8.6 hr for normal cells. The duration of pre-DNA synthetic phase of the longer cycle sub-population was significantly longer in trisomic cells.

The number of mitotic cells which succeeded cell division more than two times at 72 hr after PHA stimulation was higher in trisomic cells than in normal cells, although there was a considerable variation in the results between experiments. Furthermore, the proportion of the shorter cycle sub-population in trisomic cells was larger than that in normal cells at the time of 72 hr fixation.

There was no statistical difference between two sub-populations in the yields of chromosome aberrations by incorporated ^{3}H-TdR in each of the two cell types, but significant differences between trisomic and normal cells were found in frequencies of chromatid breaks (trisomic cells; 0.245 ± 0.023, normal cells; 0.173 ± 0.016, $p<0.025$), iso-chromatid breaks (tri.; 0.115 ± 0.021, nor.; 0.048 ± 0.018, $p<0.025$), chromatid breaks plus iso-chromatid breaks plus chromatid exchanges (tri.; 0.385 ± 0.034, nor.; 0.230 ± 0.019, $p<0.0025$), dicentrics plus rings(tri.; 0.055 ± 0.012, nor.; 0.020 ± 0.010, $p<0.025$) and the total chromosome-type aberrations (tri.; 0.238 ± 0.022, nor.; 0.153 ± 0.014, $p<0.0025$).

29. **Hidetsune OISHI** (Dept. Genet., Inst. Developmental Res., Aichi Prefectural Colony, Kasugai): **Analyses of the Break Points of Balanced Translocation Chromosomes in Man (3).**

The distribution of the points of chromosomal breakage and reunion of a series of structural rearrangements with balanced conditions was examined.

Balanced carriers with apparently normal phenotype found in 134 reciprocal translocations, 27 inversions and 5 insertions were collected from 163 published literatures and my 3 cases, and probands who were initially ascertained balanced chromosomes in these families were 56 males and females. In addition, a total

of balanced carriers found in these families was 198 of male and 257 of female. By pedigree analyses of these families, 56 fathers and 105 mothers with balanced chromosomes ascertained through phenotypically normal children with balanced conditions of chromosomes were obtained while children with balanced chromosomes from parents with the same conditions of the chromosomal rearrangement were 131 of male and 123 of female. On the other hand, *de novo* chromosomal rearrangements with these balanced conditions were detected only in 2 cases of male and 10 of female.

In a total of 322 break points identified in 166 unrelated cases the frequency of break points along chromosome length was found to be 72.1% in the negative bands, 18.0% in the positive bands and 9.9% in the variable bands. These points of breakage and reunion were not evenly distributed along chromosomes in terms of banding patterns.

Possible reasons of the apparent non-randomness of points of chromosomal breakage and exchange were discussed. Since the banding and DNA replication patterns of chromosomes in details were constant even if these chromosomal rearrangements with balanced conditions occurred and these chromosomes inherited normally through generations without any change, it was suggested that each chromosome arms were consisted of several functional units and that the break points by chromosome rearrangements with balanced conditions correspond to the terminal ends of the units.

30. **Michiko OKADA** (Dept. I Anat., Tokyo Wom. Med. Coll., Tokyo): **Chromosome Studies on Congenital Malformations and Habitual Abortions—with an Interest in Banding Pattern Analyses of Structurally Rearranged Chromosomes.**

Chromosome banding patterns were analyzed together with the conventional Giemsa-staining studies on cultured leucocytes from 45 cases of congenitally malformed children and from 8 married couples with the history of recurrent abortions and/or delivery of abnormal child.

In the former group 10 cases (8 with Down's syndrome) showed abnormal karyotypes: 6 cases with 47, XX or XY, +21, each one case with 46, XY, der(14), t(14q21q)mat.; 46, XX, t(21q21q) or i(21q); 46, XY, del(7) (q11q2105) and 46, XX, der(13), t(12; 13) (p12; q34) pat., respectively. The del(7) case, 3-month-old male, was found by the G-banding analysis to be monosomic for the proximal portion of the long arm of chromosome no. 7 (q11 and about half of q21). He showed the following clinical abnormalities; scaphocephaly, platybasia, short neck, exophthalmus, asymmetrical ears, saddle nose, high palate, cardiovascular malformation,

hypogenesis of the right lung (susp.), malformation and malposition of the right kidney, bilateral inguinal hernia, bilateral retentio testis, hypertonicity, convulsion, dyspnea, inability to swallow, and cyanosis. The infant died of a cardiac failure at 4 months. A 6-year-old girl with der(13)pat. chromosome was identified in G-banded karyotypes to 12p partial trisomy (for p12 and p13) and 13q partial monosomy (for q34) by paternal transmission of an abnormal chromosome 13 in which 13q34 was replaced with 12p12-13. In father a balanced translocation between 12 and 13 was verified. Her physical findings included severe mental and physical retardation, microcephaly, microphthalmus, hypertelorism, epicanthus, broad and rather irregular implantation of the eyebrows, prominent cheeks, small nose, small triangular mouth with thin lips, colored and irregular teeth, high arched palate, low-set ears, broad palms, club foot, rocker-bottom feet, joint hyperextensibility, hirsutism with an irregular hair stream in the back, retarded bone age in wrists, systolic murmur and status epilepticus. She died of acute pneumonia at 7 1/12 years.

In the latter group, the balanced translocation, 46, XY, t(5; 6) (q13; q22) was found in the husband whose wife experienced 6 successive spontaneous abortions and no live birth. The couple with 2 children (one healthy and the other with Down's anomaly) and 2 spontaneous abortions showed the normal karyotype, and 47, XX, +16 was identified in cultured amniotic cells obtained on the second abortion.

Clinical and cytogenetic features in above three interesting cases [del(7), der(13)-pat. and t(5; 6)] are compared with those of some reported cases showing the structural chromosome aberrations in the same chromosome members as present. Present der(13)pat. case was found to show both clinical abnormalities described in 12p trisomies and those in 13q monosomies.

31. **Shinichi MISAWA, Kimikazu SAWAI, Tatsuro TAKINO** (Dept. Int. Med., Kyoto Prefect. Univ. Med., Kyoto), **Masuji MORITA and Tatsuo ABE** (Dept. Preventive Med., Kyoto Prefect. Univ. Med., Kyoto): **Sister Chromatid Exchanges Induced by Busulfan *in vivo* and *in vitro*.**

We applied a differential staining of sister chromatids by BUdR-33258 Hoechst-Giemsa method (FPG technique) for the detection of sister chromatid exchanges (SCE's) induced by busulfan *in vivo* and *in vitro*. We studied on the incidence and the inter-chromosomal distribution of sister chromatid exchanges in normal subjects and in patients treated with busulfan in the presence of 5 μg/ml of BUdR. SCE's induced by busulfan *in vitro* were also investigated.

In control subjects, SCE's were distributed from 6.251 to 7.760 per cell and the

mean value ±2SD was 6.916±1.185. In three patients who had therapeutical application of busulfan, SCE's were from 10.129 to 11.580 and the mean±2SD was 10.979±1.154. The incidence of SCE's induced by busulfan *in vivo* were proportional to the relative chromosome length ($\chi^2=10.826$) as was observed in normal controls ($\chi^2=6.438$). A statistical significance was found in the difference of SCE's between normal controls and patients treated with busulfan ($p<0.001$).

In *in vitro* studies, cell viability in the presence of busulfan and BUdR was examined. Under the continuous medication with busulfan during the whole period of cell culture (72 hours), cell viability was almost stationary at concentrations lower than 10^{-5} mol of busulfan, but viable cells were decreased at higher than 10^{-4} mol. SCE's induced by busulfan *in vitro* were, therefore examined in the presence of busulfan at concentrations lower than 10^{-5} mol. SCE's in patients treated with busulfan almost correspond to SCE's induced *in vitro* in the presence of about 10^{-6} to 10^{-7} mol of busulfan. At concentrations lower than 10^{-9}, SCE's *in vitro* were appeared to be not affected by busulfan.

〔**質問**〕 **田村博昭** (国立大阪病院)：*In vitro* では Busulfan による SCE の頻度と dose-response curve がみられるが，*in vivo* ではこの関係が得られるのかどうか．

〔**答**〕 **三沢信一**：Busulfan 濃度と姉妹染色分体組み換えの頻度とは *in vitro* ではっきりした dose-response curve が得られた．しかし，*in vivo* で調べた3例については，その1日投与量は 1 mg, 2 mg, 2 mg，総投与量は 474 mg, 654 mg, 342 mg で，それぞれの姉妹染色分体組み換えの頻度は，核板当たり 10.129, 11.580, 11.288 と有意差はないように思われる．しかし，3例での busulfan の投与量の差が小さいので，はっきりしたことは言えない．投与を中止した後に追跡した症例はない．

〔**質問**〕 **貞森直樹** (長崎大・原研内科)：慢性骨髄性白血病症例の 60～70% の症例に急性転化時に clonal evolution を認める．これら clonal evolution をおこした症例の中には，転座や欠失等染色体レベルの異常の目立つ症例があり，busulfan が on cogenic substance として働いている可能性があるのではないか．

〔**答**〕 **三沢信一**：慢性骨髄性白血病の急性転化に，治療薬剤として使用されているアルキル化剤である busulfan がなんらかのかかわりを持っているのではないかという疑いをわれわれは持っている．Busulfan により姉妹染色分体組み換えの頻度が増加していることから，このことはさらに強く疑われるが，busulfan の直接作用として CML の急性転化が起こるのか，他の要因が付け加わって起こるのかは明らかでない．今後他の薬剤による姉妹染色分体組み換えについても検討し，明らかにしていきたい．

32. **Masuji MORITA, Tatsuo ABE** (Dept. Preventive Med., Kyoto Pref. Univ. Med., Kyoto) **and Shinichi MISAWA** (Dept. Med., Kyoto Pref. Univ. Med., Kyoto): **Demonstration of Early- and Late-Replicating Region of Human Chromosomes by Differential Staining Method.**

The present paper is concerned with the demonstration of early- and late-

replicating regions of human chromosomes. Materials comprised of cultured lymphocytes obtained by normal subjects. During first replication cycle, cells were labelled with 5-bromodeoxyuridine (BudR, final conc. 100 γ/ml medium) for two hours at 16, 12, 8 and 6 hours before metaphase and chased with thymidine (final conc. 50 μg/ml medium). Slides were made by our usual method (Abe *et al.*, 1975). They were stained with 33258 Hoechst (10^{-6} M in aqua) for 10 min. After rinsing in aqua, slides were mounted in distilled water and observed with fluorescence microscopy. Alternatively, they were stained with 33258 Hoechst (10^{-4} M in aqua) for 15 minutes and mounted in phosphate buffer, pH 8.25 and exposed to UV light for 45 minutes on the hot plate (55°C). Subsequently slides were stained with Giemsa. The mechanism involved in these techniques is that fluorescence of the dye 33258 Hoechst bound to chromosome is partially quenched by the incorporation of BudR into chromosomal DNA (Latt, 1973).

Same results were obtained from both methods. DNA replication initiated generally at negative Q-(G-)bands and terminated in positive Q-(G-)bands. Each chromosome, which had been labelled with BudR during middle phase of the S-period, had variable bands along its length, which corresponded to neither negative nor positive Q-bands. Therefore, pre-identification of all chromosomes was required for the identification of each replicating regions of each chromosome. Thus, chronological order of DNA synthesis of human chromosome, which otherwise had been inadequately given by autoradiographic method, could be demonstrated by the banding method. The detail will be published elsewhere.

33. **Hachiro SHIMBA, Kazuo OHTAKI and Toshio SOFUNI** (Dept. Clin Labs., RERF, Hiroshima): **The Sites of Breakage of Radiation-Induced Chromosome Aberrations, Determined by the G-Staining Method.**

The development of banding techniques for the specific identification of individual chromosomes as well as chromosome regions has offered an opportunity to study, in much detail, the site at which radiation-induced damage occurred in human chromosomes.

We present results of an analysis of breakpoints of chromosome aberrations examined by the trypsin G-method in peripheral blood obtained from a non-exposed healthy male exposed to Co^{60} gamma-rays *in vitro*. Chromosome slides were first prepared by ordinary Giemsa stain and well spread metaphases were photographed. The same slides were treated with trypsin then for the G-bands. Karyotype analyses were made on the same metaphases by both ordinary and G-staining methods.

135 cells (43.7%) of the 309 thus analyzed were found to have 186 radiation-

induced aberrations; one tricentric, 63 dicentrics, 46 translocations, 20 complex aberrations, 11 rings, 7 inversions, 20 acentrics and 18 deletions. A total of 354 breakpoints were identified in these 186 aberrations. Of them, 287 breakpoints involving tri- and dicentrics, translocations and complex aberrations were used for the analysis of distribution of breakpoints between chromosomes. A comparison of the number of breakpoints observed in each chromosome with the expected values on the basis of chromosome length gives $\chi^2=16.72$, (d.f. 23, $p>0.5$). Present result suggests that the distribution of breakpoints of radiation-induced aberrations is proportional to the length of individual chromosome.

34. **Kazuo OHTAKI, Hachiro SHIMBA, Masashi HIRAMOTO and Toshio SOFUNI** (Dept. Clin. Labs., RERF, Hiroshima): **Radiation-Induced Chromosome Aberrations in A-bomb Survivors by Trypsin G-banding Method.**

It has been suggested that a part of radiation-induced chromosome aberrations was not detected by ordinary staining method but by the use of new banding techniques. In our previous report, some of the exchange aberrations found in peripheral lymphocytes of A-bomb survivors were only identified by the trypsin G-staining method. We present here further cytogenetic findings from 23 A-bomb survivors in whom high frequency of aberrant cells were noted in the previous examination.

Slides were stained by ordinary method, and metaphases suitable for karyotype analysis were photographed, and then the same slides were processed for G-method so that the G-banding patterns of the previously analyzed metaphases could be reexamined. Karyotype analyses were carried out separately by each of the two methods in the same metaphase. Types and frequencies of chromosome aberrations

Comparison of the frequencies of cells with radiation-induced chromosome aberrations between ordinary and G-methods.

Ordinary method	G-method	Number of cells
Normal	Normal	548
Aberrant	Aberrant	287
Normal	Aberrant	55
Aberrant	Normal	6
	Total cells examined	896
Aberrant cells	Ordinary method	293 (32.7%)
	G-method	342 (38.2%)

were compared between the two methods.

A total of 896 cells were examined, and frequency of aberrant cells was found to be 32.7% by the ordinary method, while it was 38.2% by the G-method. 55(16%) out of the 342 aberrant cells detected by G-method were found impossible to identify by the examination of ordinary method. Of these 55 cells, 17 showed to have a translocation of equal length of chromosome segments, and in 9 a paracentric inversion was observed. The remaining aberrations were various types of translocations and inversions that were not identified simply by the current method. Six cells were identified as abnormal by ordinary method, whereas they were found to show normal band pattern. This was partly due to partial shrinkage of chromosomes by ordinary method.

35. **岡　成寛・中込弥男**（遺伝研・人類遺伝）：**DNA 複製パターンに基づく多型染色体の研究.** Shigehiro OKA and Yasuo NAKAGOME (Nat. Inst. Genet., Mishima): **DNA-Replication Pattern in the Detection of Chromosomal Polymorphism.**

ヒト染色体の多型現象の解析には，従来主にCおよびQバンド法が使われてきた．Cバンド法は，標本作製・処理条件等により，濃染部の大きさが大きく変化するため，定量的な扱いは不可能である．Qバンド法は，処理条件によるバラツキは少ないが，1; 9; 16番などの二次狭窄部の多型型・端部着糸型染色体の短腕で螢光の弱いものなどの判定が，きわめて困難である．そこでわれわれは DNA 複製パターンに基づいて，染色体の多型部分を客観的に評価することを試み，実用化の見通しを得たので概要を報告した．

方法：①培養終了24時間前 5-bromodeoxyuridine (BudR) 加（最終濃度 10^{-4} M）以後遮光培養．②培養終了8～6時間前に新しい培養液で細胞を洗浄．その後サイミジン（最終濃度 1.2×10^{-5} M）加の培養液と交換．培養液はあらかじめ 37°C に温め，pH も調整しておく．③培養終了2時間前コルセミド加（最終濃度 0.07 γ/ml）．④型のごとく標本作製．⑤アクリジン・オレンジ（10%シュレーセン緩衝液5分）で染色後，螢光顕微鏡で観察・写真撮影．

結果：1; 9; 16番染色体の二次狭窄部は，すべて強い螢光を発するため，容易に識別できるほか，処理条件の差によるバラツキもきわめて少ない．その結果，真正染色質の長さを基準として二次狭窄部の長さを表わし，多型所見を，例えば +2 標準偏差といった形で取扱うことが可能となる．正常値については現在症例を増して検討中である．また，端部着糸型染色体の短腕は，Qバンド法によると螢光が弱く判定困難な場合が多いが，本法によるとほとんど総て強ないし中等度の螢光を発するため，大きさないし螢光の強さにもとづいて確実に分析できることが明らかとなった．

〔**質問**〕 **塩見敏男**（長崎大・原研遺伝）：新しいテクニックとして，大変有用なものと考えられるが，再現性の点に関して如何．

〔**答**〕 **岡　成寛**：今回の方法によるものは，二次狭窄部の大きさ（ヘテロクロマチン部）に，標本作製後の日数等によってのバラツキがほとんどみられないので，再現性は十分あると思われる．

36. **Kazuzo IINUMA, Ei MATSUNAGA** (Dept. Hum. Genet., Nat. Inst. Genet., Mishima), **and Tatsuhiro YAMANAKA** (Dept. Pediat., Ensyu Sogo Hosp., Hamamatsu): **Studies on Q-Polymorphisms in an XX/XY Individual and Cytogenetic Evidence for Double Fertilization.**

A 4-month-old infant with ambiguous genitalia was referred to our laboratory for cytogenetic assessment. Chromosome analysis on leukocyte cultured revealed a sex chromosome mosaicism, 46, XX/46, XY in a proportion of 4 : 1. In buccal mucosa cells, X-chromatin was positive in 51% nuclei and Y-chromatin was positive in 10% nuclei. Some of the granulocytes, lymphocytes and monocytes in blood smears had a Y-chromatin. Laparotomy had not been performed. Karyotypes of the parents were normal. Blood groups of the patient, mother and father were B, M, P_1, R_2R_2, $H_p(2\text{-}2)$; AB, M, P_1, R_1R_2, $H_p(2\text{-}1)$; and B, MN, P_2, R_2R_2, $H_p(2\text{-}2)$, respectively. As for the patient, there was no direct evidence of blood group chimera. Q-Banding studies in the family revealed that (1), in the patient, the combination of the Q-variants of chromosome number 21 in XX cells was not similar with that in XY cells and (2) the mother had a brilliantly fluorescing paracentromeric region in one of the chromosomes number 3, but neither of the father and the patient had such a "marker" chromosome. From these results, we postulated that an XX/XY zygote might be produced through a double fertilization of either an ovum and a second polar body or two haploid nuclei, daughters of the ovum nucleus. Another possibility was that two independent zygotes may have fused in a blastocyst stage, this event having been observed in mice.

37. **Shinichiro NANKO** (Inst. Brain Res., Univ. of Tokyo Sch. of Med., Tokyo): **Frequencies of Y Chromatin Positive Lymphocyte in Males.**

Frequencies of positive Y chromatin leucocyte are known to vary from 60% to 80% but to depend upon the time after fixation of the blood smear (Hashi and Usui, 1972; Yanagisawa, 1973). The present, subjects are 351 males (13-19 years of age) and in each case 50 lymphocytes were examined in blood smear with quinacrine mustard staining. The average frequency of Y chromatin positive lymphocytes was 59.4% (Edge 33.5%, Center 25.4% and Double 0.5%). There is a tendency that the frequency decreases with the days after fixation. After angular transformation, the regression equation upon days after fixation is given by $Y=-0.42X+52.9$ ($t=6.50$, d.f.$=349$, $p<0.01$). The correlation coefficient is also significant ($|r|=0.25$, $p<0.01$).

38. **Toshio SOFUNI, Junso NARUTO and Akio A. AWA** (Dept. Clin. Labs., RERF, Hiroshima): **Chromosome Polymorphisms in a Human Population Ascertained by C-staining Method.**

In our previous report, polymorphisms of human chromosomes detected by the C-staining method have been found to occur with relatively high frequencies. Since data about chromosome variants identified by the C-method have been accumulated to data for about 1,000 randomly selected Hiroshima residents, we summarize here results on the type and frequency of such variants. Subjects studied were selected from among those participating the RERF Adult Health Study Sample (AHS) comprising A-bomb survivors and non-exposed controls, and from among the offspring of A-bomb survivors and their controls (F_1). A total of 993 persons have been so far examined, comprising 421 AHS and 572 F_1 participants (450 males and 543 females).

One of the most characteristic polymorphic patterns identified by the C-method was a pericentric inversion of a No. 9 chromosome, found in 11 individuals (1.1%); 6 (1.4%) in AHS and 5 (0.9%) in F_1. Six persons (0.6%) were found to have an extra band in the proximal region of the short arm of a No. 1 chromosome (1ph+); 4 (1.0%) in AHS and 2 (0.3%) in F_1. 1qh+ was found in 8 persons (0.8%); 4 from

Number of cases with chromosome variants ascertained by C-staining method.

	AHS 421	F_1 572	Total 993
inv(9)	6	5	11
ins(Y)	1	—	1
1ph+	4	2	6
1qh+	4	4	8
4qh+	1	—	1
5ph+	1	1	2
6ph+	2	1	3
9qh+	2	1	3
11ph+	—	1	1
12ph+	2	2	4
14ph+	—	1	1
14sh+	—	1	1
15ph+	4	5	9
15sh+	—	1	1
16qh+	3	3	6
22ph+	—	1	1
Total	28 (6.7%)	28 (4.9%)	56 (5.6%)

each two samples. Nine were found to have a large band in the short arm of a No. 15 chromosome (15ph+). Six cases with 16qh+ were also identified, and 9qh+ were found less frequently, *i.e.*, in 3. There were 3 individuals having two variant chromosomes identified by the C-method. Together with other variants (see Table), a total of 56 persons (5.6%), 28 (6.7%) in AHS and 28 (4.9%) in F_1, were found to show chromosome variants detected by the C-method. There was no significant difference in frequency of the variants between males and females. (This study was supported in part by the Research Fund from the Ministry of Health and Welfare (1976))

39. **Kimio FUJITA and Hiroko M. FUJITA** (Cytogenetic Laboratory, Saku Central Hospital, Minamisaku Usuda, Nagano): **Cytogenetic Studies in the Rural Population.**

Cytogenetic studies were performed on the peoples living in a rural village in Nagano Prefecture. Peripheral venous bloods were obtained between December 1974 and March 1975. Leukocytes were cultured for 60 hours. Colchicine were added 2 hours before harvesting. Up to the present, 3,754 mitotic figures from 393 persons were observed.

There were no aneuploidy persons. None was found to carry an abnormal chromosome. Persons with an abnormally high breakage frequency were not found. Chromosomal aberrations, such as breaks, fragments, deletions, bridges and exchanges, were scored as abnormal and breakage frequencies were calculated. Persons were classified into two groups, farmers and non-farmers. The farmers in the age groups of 30-39 year and 40-49 year showed higher breakage frequencies than the frequencies shown by the other age groups. Summing up, the breakage frequency of the farmers in the ages of 30 to 49 year were 0.03711 (18/485) and that of others was 0.02141 (70/3269).

This is an interim report. If the difference between the two groups is significant, a variety of herbicides, insectcides and fungicides may be suggested as the causative factors as Japanese farmers are heavy users of these agents.

〔**質問**〕 **田村博昭**（国立大阪病院）：Breakage rate の算出方法を教示願いたい.

〔**答**〕 **藤田公生**：今回は chromatid type, chromosome type あるいは one-hit, two-hit の区別をせずに one break とした. 観察細胞数が増えたら, さらに切断の内容を検討してみる.

40. **Yujiroh KAMIGUCHI, Kenji FUNAKI and Kazuya MIKAMO** (Dept. Biol. Sci., Asahikawa Med. Coll., Asahikawa): **A New Technique for Chromosome Preparation of the Murine Oocytes.**

Chromosome analysis of gametes or early zygotes is one of the most important

means for searching for the etiologic factors of chromosomal anomalies, as well as for understanding their causal mechanisms. Although Tarkowski's method has been applied by many investigators to analyze chromosomes of the eggs of various mammalian species, his technique tends to induce loss or scattering of chromosomes, which is caused by rupture of the cell membrane either at the moment of application of fixative or during the drying process.

We developed a new technique for the secondary oocyte of the Chinese hamster in order to obtain a proper spreading and reliable maintenance of the chromosomes within the ooplasm. Eggs were recovered from oviducts and treated with the following procedure. To remove the cumulus oophorus cells and simultaneously to weaken the zona pellucida, the eggs are treated with 0.5% trypsin for 1.5 minutes. The denuded eggs are then treated with 30% calf serum for 60 minutes at 37°C to disperse the chromosomes completely within the ooplasm. After this treatment, the eggs are fixed gently with fixative I (methanol: acetic acid: H_2O=5 : 1 : 4) for 5 minutes. A single egg, together with a small amount of the fixative, is sucked up into a Spemann pipette with a fine point, then pushed out on a grease-free slide. While the fixative spreads, the egg sticks to the slide near the tip of the pipette. The egg is re-fixed and tightly stuck there by an immediate application of fixative II (methanol: acetic acid=3 : 1). The slide is put at once into a coplin jar filled with the same fixative and kept there for 20 minutes or more. The slide is then dipped into a fixative III (methanol: acetic acid: H_2O= 4 : 3 : 1) for 1 minute to help the egg flatten during the next drying process. The slide is removed very slowly from the fixative and dried with the air which is moisturized by passing through water at 37°C. Throughout the procedure handling and observing of the eggs are performed under the binocular dissecting microscope.

Out of 1,498 hamster eggs collected from 204 females, 1,265 (84.4%) were karyotyped successfully. In these slides the chromosomes were properly spread and surely maintained within the flattened ooplasm. Remaining 233 eggs (15.6%) were not analyzed due to accidental loss, rupture of egg cell membrane, or splitting and overlapping of chromosomes. About 45% of those not analyzed had already been degenerative at the time of collection. Therefore, the rate of success of this method may be estimated over 90%.

With the same procedure, primary oocytes of the hamster and the mouse were also prepared satisfactorily. Moreover, this method was found to be applicable, with a slight modification, to early zygotes of the hamster and the rat. This technique may be useful to investigate possible correlations between chromosomal

aberrations and various teratogenic factors, such as aging of the ovum, radiation, certain chemical substances, etc.

〔質問〕 **菊池康基** (武田薬品・中研) : Aid dry 法を具体的に教えてほしい.

〔答〕 **上口勇次郎** : Air-pump より送り出した空気を 37°C の water bath の中を通して加湿温風としたものを一定の口径をもつノズルからふき出させ, 一定の距離の位置にスライドを立てて乾燥させる. 加湿温風は, 卵細胞質を均一に扁平乾燥させるうえで重要である.

〔質問〕 **阿波章夫** (放影研, 広島) : 標本作成上の失敗例にはどのようなものがあるのか, うかがいたい.

〔答〕 **上口勇次郎** : 失敗した 15% の中の多数の卵は採卵時にすでに種々の形態的異常の認められたもので, 卵自身の原因によって卵細胞膜が破壊しやすかった例である.

41. **Norio WAKE, Nobuo TAKAGI and Motomichi SASAKI** (Chromosome Res. Unit, Fac. Sci., Hokkaido Univ., Sapporo): **Non-Random Inactivation of X Chromosome in the Rat Yolk Sac.**

The Lyon hypothesis (Lyon, 1961) postulates that the mammalian female is a natural mosaic for clones of cells with either the maternally derived X chromosome (X^m) or the paternally derived one (X^p), which is randomly inactivated early in development. We have presented (Takagi and Sasaki, 1975) evidence for the dominance of the inactive X^p in extraembryonic regions of 7.5- and 8.5-day mouse embryos heterozygous for Cattanach's translocation in which the two X chromosomes could be readily identified. Though it was presumed that this might not be an exceptional phenomenon restricted to mice bearing this X-autosome translocation, this has been difficult to confirm because of the lack of a system suitable for experiments. Here we report further cytological evidence that the inactive X is predominantly paternal in the yolk sac of the laboratory rat.

We used X^t-X^{st} dimorphism in the laboratory rat (Hungerford, 1963); the X chromosome is telocentric (X^t) in F344 and ACI strains, whereas it is subtelocentric (X^{st}) in WKA strain at our laboratory. X^tX^{st} heterozygotes were obtained from the cross ACI (X^tX^t)×WKA ($X^{st}Y$) and WKA ($X^{st}X^{st}$)×F344 (X^tY). Embryos were recovered from the decidual swelling at 10.5 gestation, and mosaic composition was studied only in the embryo proper and yolk sac by means of an acridine orange fluorescence technique after BudR incorporation (Takagi and Sasaki, 1975).

Cytogenetic examination was carried out in 8 and 7 female embryos from the cross $X^{st}X^{st}\times X^tY$ and $X^tX^t\times X^{st}Y$, respectively. Distinction between X^{st} and X^t was unequivocal and an asynchronously replicating X was identified as the palest red element in the great majority of metaphase spreads with banded chromosomes. In the former 8 embryos the percentages of cells with the X^p allocyclic ranged from 82.1% to 97.8% with an average of 94.7% in the yolk sac, whereas it ranged

from 46.7% to 71.4% with an average of 55.3% in the embryo proper. Difference between the two was highly significant ($p<0.001$). The results were similar in the latter 7 embryos. It seemed that there was more variation in mosaic composition among embryos themselves than yolk sacs, as indicated by a significantly higher standard deviation ($p<0.05$).

There are at least three possible ways of explaining the predominance of cells with the X^p allocyclic in the yolk sac; (1) reactivation of the inactive X^m with simultaneous inactivation of the active X^p, or (2) selective growth of cells with the X^m active after random inactivation or selective sampling for cells with X^m active in primordial cells of extraembryonic membrane; (3) preferential inactivation of X^p. But resolution of this problem will require fuller cytological studies of embryos in early development.

42. **Yujiroh KAMIGUCHI, Kenji FUNAKI and Kazuya MIKAMO** (Dept. Biol. Sci., Asahikawa Med. Coll., Asahikawa): **Chromosomal Anomalies Caused by Intrafollicular Overripeness in the Early Zygotes.**

In has been well known that various developmental anomalies are induced by intrafollicular or preovulatory overripeness of oocytes caused by delayed ovulation. Mikamo and Hamaguchi (1975) observed a highly significant increase of diandric triploidy in 1-cell rat embryos in a cytogenetic study of the effect of delayed ovulation. Butcher and Fugo (1967) first noticed that aneuploids and mosaics might increase in the 11-day embryos developed from preovulatory overripe eggs. Later, Mikamo and Hamaguchi (1975) found a much stronger effect of the delayed ovulation on the chromosomal aspects of preimplantation blastocysts, although their material was not large enough in number to prove statistical significance. Even in such an early developmental stage a great number of embryos of the delayed ovulation group were not analyzable karyologically due to declined mitotic activity. This fact suggests that earlier developmental stages may better fit the chromosomal study of the effect of delayed ovulation. In the present study we investigated two-cell embryos, using a new chromosome technique which was developed by the authors for the study of murine eggs (Kamiguchi, Funaki and Mikamo, 1976).

Ovulation was delayed for 48 hours in sexually mature female rats (Wistar-Imamichi strain) with repeated injections of pentobarbital sodium (30 mg/kg body weight) on successive two days (at 1: 45 p.m. on the day of proestrus and at 1: 00 and 1: 45 p.m. on the day of estrus). Two-cell embryos were collected from oviducts 2.5 days after fertilization and prepared for chromosome analysis.

A significant increase of chromosome anomalies in the delayed ovulation group was confirmed in a rather small number of specimens. There were 8 cases of polyploids (8 triploids) in 281 embryos of the control group, while 29 polyploids (25 triploids, 3 tetraploids and 1 pentaploid) in 280 embryos of the experimental group. These polyploids were all ascertained to be polyandric by counting the number of the tail remnants of fertilized sperms. The difference between two groups was highly significant ($p<0.001$). Thus, earlier finding of Mikamo and Hamaguchi (1975) was confirmed. Both aneuploids and mosaics also increased significantly in the delayed ovulation group ($p<0.05$). Five aneuploids (3 monosomy and 2 trisomy) were observed in 272 control embryos, whereas 14 aneuploids (9 monosomy and 5 trisomy) in 251 treated embryos. Similarly, 5 mosaics (1 case of 42/43, 1 case of 41/42, 2 cases of 41/43 and 1 case of 39/45) were found in the control group, whereas 13 mosaics (4 cases of 42/43, 3 cases of 41/42, 5 cases of 41/43 and 1 case of 39/42) in the delayed ovulation group.

These results indicate that intrafollicular overripeness of the oocyte after delayed ovulation causes polyspermy and nondisjunction or anaphase lagging of chromosomes during the meiotic divisions and as well as during the first cleavage division.

43. **Sadayuki BAN, Tsutomu SUGAHARA** (Dept. Exptl. Radiol., Fac. Med., Kyoto Univ., Kyoto), **Fumio SUZUKI and Masakatsu HORIKAWA** (Div. Radiat. Biol., Fac. Pharmac. Sci., Kanazawa Univ., Kanazawa): **Genetic Studies of Somatic Mammalian Cells *in vitro*. Sensitivity and Utility of the Mutagenesis Systems.**

The investigation of mutagenesis at the cell level is very important for elucidating the genetic hazards of environmental mutagens in man. Recently, we have obtained a prototrophic (Ala^+, Asp^+, Pro^+, Asn^+, Hyp^+, Glu^+)- and an auxotrophic (TdR^-)-clone from the cultured Chinese hamster *hai* cells by appling our replica plating method. Furthermore, we have isolated 8-azaguanine resistant cells from 8-azaguanine sensitive cells (prototrophic clone). With these cells we have constituted the model systems for mutagenesis testing as follows:

I. Forward mutation system
   (a) prototroph ⟶ auxotroph (b) 8-azg^S ⟶ 8-azg^R
II. Reverse mutation system
   (a) auxotroph ⟶ prototroph (b) 8-azg^R ⟶ 8-azg^S

By comparing mutation frequencies induced by various doses of X-ray, UV-ray, 4-NQO, MNNG and EMS, it was indicated that system I(a) is the most sensitive to detect the mutagenecity of all mutagens used and system I(b) is the most

insensitive. By using system I(a) the mutagenecity of AF-2, which had been widely used as a food preservative, and Elkind type recovery of mutational damage for X-rays were clearly demonstrated.

A preliminary study in normal human embryonic cells is now under by using a similar method.

44. **Toshio SHIOMI and Isao YOSHIKAWA** (Dept. Genet., Nagasaki Univ. School of Med., Nagasaki): **Genetic Investigations in Nagasaki Atomic Bomb Survivors. 1. The Outline of Subject Population and F_1 Sex Ratio.**

With the purpose to investigate the possible genetic effects of Atomic-bombing radiations on the Nagasaki residents, a study sample population was established on the basis of registration cards of A-bomb survivors keeping in the Nagasaki City Office. The number of registrated survivors as of Dec. 1973 had been counted up 97,032 (39,840 men and 57,192 women). Among those, 83,008 peoples were present in the area within 10 km of the hypocenter at the time of the bombing (ATB). The most of remainders were the early entrants in the City after the bomb explosion.

For convenience, let the study samples applicable to the possible genetic study be constituted from survivors less than 46 years old ATB, the number of all survivors extracted from the registrations are 28,922 men and 44,255 women. A primary population of the genetic study was made up of the all survivors less than 21 years old ATB and belonged to the next two groups:

Group I ---- exposed within 1,500 m of the hypocenter.

Group II ---- exposed more than 5,100 m of the hypocenter.

These distances from the hypocenter are based on the description of registration cards. As the card distance was given roughly by the administrative boundary, the more exact distance was estimated with the data of exposure location for each survivors and the restoration map of the City ATB. The sampled numbers in Group I are 2,547 (1,252 men and 1,295 women), and those in Group II are 2,791 (1,344 men and 1,347 women).

Exposed air dose of each survivors was calculated according to the following equation based on the data estimated by Hashizume and Maruyama (1975);

$$\text{Exposed Dose}=\frac{59731.795}{1.0042325^{D}}\times S_g+\frac{11094.651}{1.0052202^{D}}\times S_n$$

where D is the estimated distance (m) from the hypocenter, and S_g and S_n are the shielding factors for Gamma-ray and Neutron. These values are as follows;

	S_g	S_n
Unshielded	1.00	1.00
Lightly shielded	0.81	0.35
Heavily shielded	0.50	0.30

Using the koseki (family registration), the following items were inquired for each survivors: 1) Life history and pedigree up to P_3-generation about each survivors and his (or her) spouse, 2) Birth history about offspring of each couples. In addition, the exposure status for the spouses was checked up.

The sex-ratio for F_1 was investigated in relation to their parent's exposure status to the A-bomb. The change in sex-ratio for father's exposure were in direction to be expected if exposure had induced sex linked lethal mutations ($0.05>p>0.10$ for χ^2, d.f.$=2$). However, that for mother's exposure did not distinctly changed.

A detailed analysis of this results is now in progress.

45. **Toshio SHIOMI and Toshiaki MATSUMURA** (Dept. Genet., Nagasaki Univ. School of Med., Nagasaki): **Genetic Investigations in Nagasaki Atomic Bomb Survivors. II. Chromosome Aberrations in Somatic Cells of the A-bomb Survivors.**

Chromosomes of one hundred and fifty-five exposed Nagasaki Atomic Bomb survivors have been investigated. 95 persons were inner proximal exposed, within 1,400 meters of the hypocenter (H group), and 60 were distally exposed, more than 2,500 meters (C group).

Lymphocytes of peripheral blood samples were cultured for 48 hours at 37°C and 100 metaphase plates from each subjects were examined microscopically, and confirmed by photographic negative film projection method and photographs were subjected to karyotypic analysis. There are no notable differences in the frequencies of modal diploid cells or cells with single- and iso-chromatid gaps and breaks for both groups. Similarly, the frequency of cells with unstable type chromosome aberrations (Cu) did not differ significantly between H and C groups. On the other hand, frequency of cells with stable type (Cs) or exchanged type (Ex) chromosome aberrations are about four times greater in H than C. Presence of these aberrations means the effect of A-bomb radiations still remains even now more than 30 years after exposure.

Percentage of cells with chromosome type aberrations

Group	C	H
Cells	6,000	9,383
Cu	0.68	0.72
Cs	1.05	4.54
Cu+Cs	1.58	5.13
Ex	1.10	4.21

Furthermore, analyses of the data on the chromosome type aberrations were performed with following standpoints.

1. Exposed distance cited from the survivor's registration card (card distance).
2. Exposed distance estimated from the interview data on the location of subject ATB.
3. Radiation dose estimated from the distance and exposure status for each subject.

In each cases, frequencies of Cu type cells are not so changed with distances and doses. On the other hand, Cs type or Ex type aberrations vary inversely as the exposed distance or proportional to the estimated dose.

Percentage of aberrant cells and estimated dose

Group	C		H	
Dose (red)	<3	0-150	150-250	250<
Cells	6,000	5,400	2,442	1,541
Cu	0.68	0.59	0.82	1.04
Cs	1.05	2.41	4.75	11.68
Cu+Cs	1.58	2.94	5.36	12.39
Ex	1.10	2.28	4.50	10.51

46. **浅香昭雄**（東大・脳研），**松井一郎**（神奈川こども医療センター），**開原成允**（東大病院・電算機企画室）：**Down 症候群の皮膚紋理による判別分析.** Akio ASAKA (Inst. Brain Res., Univ. Tokyo, Tokyo), Ichiro MATSUI (Kanagawa Child. Med. Center, Kanagawa) and Shigekoto KAIHARA (Computer Cent., Tokyo Univ. Hosp., Tokyo): **Discriminatory Analysis of Dermatoglyphics of Down's Syndrome.**

Down 症候群を皮膚紋理によって臨床的に判別する試みとして，すでにいくつかの方法が報告されているが，われわれは，Down 症候群 (Down) 251 名（男 140，女 111），正常対照群 (Control) 302名（男 167，女 135）の皮膚紋理特徴 28 items を検べた．その中 item 1～10 は 10 指の紋理の分類 (W, U, R, A)，11～16 は左右第 2, 3, 4 指間紋の有無，17～20 は左右小指球紋と母指球紋の有無，21，22 は左右三叉線の位置 (t, t′, t″)，23，24 は左右猿線の有無，25，26 は左右第 5 指単一屈曲線の有無，27, 28 は左右足母指球紋理の分類（遠位蹄状紋など 6 カテゴリー）である．以上の 28 items の 2 ないし 6 カテゴリーについて，Control (P) と Down (P′) の出現率(数) を求め，以下

の数値を求めた. (A) odds ratio の対数, $\ln\left(\frac{P'}{1-P'}\Big/\frac{P}{1-P}\right)$, (B) それぞれの尤度比の比の対数 (原理は Borgaonkar (1971) の方法と同じ, log odds ratio と呼ばれている), の2つである. 各個体にそれぞれのカテゴリーに相当する値をいれかえ数量化を行なった. 28 items の和の平均値をみると, (A) Control −28.44±10.74, Down 14.02±13.14, (B) Control −11.84±6.08, Down 13.87±7.56 であった. 次に各 item の値を変数とした判別関数分析を行ない, それぞれの正診率は (A) Control 96.02% (290/302), Down 97.60% (245/251), (B) Control 96.35% (291/302), Down 98.40% (247/251) をえた. 判別値の平均は (A) Control −13.01±4.44, Down 7.01±4.51, (B) Control −8.54±4.59, Down 11.40±4.30 であった.

47. **Reiko HARADA, Kazuyuki ISHITOBI, Tetsuhiro NINOMIYA, Yasunobu SANTO and Yoshimichi HARADA** (3rd Dept. Med., Tottori Univ., Yonago); **Mosaic Turner's Syndrome and the Dermatoglyphics.**

In Turner's syndrome of 14 cases with 45, X cell types and 19 cases with mosaic types (45, X/46, XX; 45, X/46, X, i(Xq); 45, X/47, XXX; 45, X/46, X, r(X); 45, X/46, X, minute X; 45, X/46, XX/47, XXX), the difference of dermatoglyphic features between right and left hands was investigated for the finger ridge count, the maximal atd angle and the a-b ridge count. The controls were 110 healthy females.

Finger ridge count: In 45, X subjects, the mean difference of the ridge counts between right and left hands (R minus L) was 6.7±4.6, and the correlation ϕ coefficient (r) between right and left hands was 0.943. In mosaics, the mean was 9.3±5.8 and r was 0.919, and in controls 7.2±5.0 and 0.935, respectively.

Maximal atd angle: In 45, X subjects, the mean of the atd angle (R minus L) was 3.7°±3.8° and r was 0.513. In mosaics the mean and r were 5.7°±4.7° and 0.580, and in controls 2.5°±3.0° and 0.751, respectively.

a-b ridge count: In 45, X subjects, the mean difference of the a-b ridge count (R minus L) and r were 5.1±2.6 and 0.636, in mosaics 3.1±2.6 and 0.636, and in controls 2.5±1.9 and 0.751, respectively.

Finger print pattern: In Turner's syndrome, the frequency of the ulnar loop (U) was higher and whorl (W) was lower than those of control females. In mosaics the frequency of W and U on both hands were similar to those of 45, X subjects, but on the right hand U appeared more and W less frequently than on the left hand. The difference between both hands was more than 10%.

Usually, dermatoglyphic traits show a similarity between right and left, but it is decreased by chromosome abnormalities. The value of difference between both hands, right minus left, was more variable in mosaics than in normal females. In 45, X cell types, a larger variability was observed than in control females and

it was intermediate between controls and mosaics. As Polani *et al.* stated, present findings that mosaics were most variable in these three populations might be caused by uneven distribution of more than two cell lines and different proportion of these cell lines. The lesser degree of asymmetry in dermatoglyphics in the 45, X subjects than the mosaics suggests the existence of mosaicism which might be overlooked in the non-mosaic subjects.

〔質問〕 **塩野 寛**（国立西札幌病院）：1) Mosaic 型の Turner 症候群の総隆線数，a-b 隆線数がともに XO Turner 症候群より高く出ているが，理論的には正常と XO Turner 症候群の間にくるのではないか．

2) 主線Aが母指球部に終る頻度はどのくらいか．

〔答〕 **原田礼子**：症例数が少ないこと，様々なモザイク型を一集団として取り扱ったことで，誤ったデーターになったかもしれないが，モザイク型において，総隆線数が最も高かった．両親の影響かもしれない．

48. **Hiroshi SHIONO and Jun-ichi KADOWAKI** (Dept. Pediat., National Nishi-Sapporo Hosp., Sapporo): **Dermatoglyphics in Cri du Chat Syndrome.**

The dermatoglyphics of 33 Japanese patients with Cri du Chat Syndrome (20 females and 13 males), which were reported in literature including four cases of the author's observation) were compared with 544 male and 129 female controls. Eighteen cases were, however, described on only simian crease and distal axial triradius. These patients showed a higher incidence in characteristics such as the whorl and arch pattern on the finger apex, the thenar pattern, the bilateral appearance of the simian crease and the distally displaced axial triradii on both palms (t′).

49. **Yuko NAGANO** (Dept. Pediat.. Kyushu Univ., Fukuoka), **Koji UEDA** (Shool of Health, Kyushu Univ., Fukuoka), **Yoshikazu KUROKI** (Kanagawa Children's Medical Center, Kanagawa), **Nagahide GOYA** (Dept. Pediat., Kyushu Univ., Fukuoka): **Dermatoglyphics in the Congenital Rubella Syndrome.**

Dermatoglyphic study was performed in 38 girls with congenital rubella syndrome in Okinawa Prefecture and their mothers as controls. One girl had congenital heart disease, cataract, retinopathy and deafness. Seven girls had congenital heart disease, retinopathy and deafness. Thirty girls had retinopathy and deafness. The girls were divided into two groups, CHD group and CHD-free group, according to the presence or absence of congenital heart disease. Following findings were obtained in CHD group: 1. increased incidence of digital whorl patterns and decreased incidence of digital loop patterns, 2. increase in the pattern intensity on the first, the third, the fourth and the fifth fingers, 3. decrease in the a-b

ridge count, 4. decreased incidence of true patterns in the fourth interdigital space, 5. increase in the main line index, and 6. no significant difference in the total ridge count, thenar pattern, hypothenar pattern and palmar flexion crease.

No significant differences were recognized in CHD-free group.

The combination of the congenital heart disease and the dermatoglyphic changes shows the overlapping of the periods, when the heart and the dermatoglyphic patterns have been malformed by rubella infection. Therefore, it is thought that the dermatoglyphic changes by rubella infection are completed within the first three months of gestation as congenital heart disease.

50. **M. OKAJIMA** (Dept. Forensic Med., Tokyo Med. and Dent. Univ., Tokyo): **A Genetic Study of Epidermal Ridge Minutiae.**

In recent years, biological interest in epidermal ridge minutiae has been aroused, though technical difficulties still remain. In earlier studies, minutiae were classified into many complex forms and compared in homologous sites between parents and children and between monozygotic twins. The results, however, could not reveal genetic effects on this trait (Steffens, 1965). On the other hand, Okajima (1966, 1967) proved that the occurrence of simple forms of minutiae, *i.e.*, ends, forks, islands and short breaks, are determined to some degree by heredity, as relatively high correlation coefficients were obtained in monozygotic twins in the frequency of minutiae in the calcar area as well as in the proportion of forks in total minutiae in the hypothenar area of the palm.

In the present paper, the proportion of forks (fork index) was studied in the hallucal area in 75 male and 72 female Japanese students between the ages of 14 and 16, and 99 pairs of twins of 12 years of age. In the student sample, the mean of fork indices for males was 6.67 ± 0.56 in the right and 6.25 ± 0.56 in the left, and for females 5.31 ± 0.36 and 5.49 ± 0.45, respectively. Bilateral and sex differences are not evident. The mean fork index was slightly but statistically significantly different in the two samples and the effect of age on this trait, which might closely relate to the printing technique, is conceivable. The correlation coefficient, 0.75 ± 0.06, for monozygotic twins is higher than 0.56 ± 0.20 for like-sexed dizygotic twins and 0.41 ± 0.34 for unlike-sexed twins, though the difference is statistically not significant because of small number of dizygotic twins. From the results presented here and in the previous paper, it may be concluded that the formation of complex forms of minutiae is not under the control of heredity, while the occurrence of simple forms of minutiae is determined to some extent genetically. The details of this study will be published in Mitteilungen der Anthropologischen Gesellschaft

in Wien.

〔質問〕 **浅香昭雄**（東大・脳研）：Fork index の部位間の相関の有無について.

〔答〕 **岡島道夫**：詳しくは調べていないが，指紋では同一個体の指の間にある程度の正の相関がみられる.

51. **Kazuo MIYOSHI, Yasunori KAWACHI, Toshinao YAMANO, Michiyo OJIMA, Seiji KOKAWA, Muneo SUZUKI and Fumitoshi OHNO** (Dept. Int. Med., Tokushima Univ., Tokushima): **Trisomy Mosaicism Demonstrated in Familial Chronic Thyroiditis.**

Trisomy mosaicism of various patterns was demonstrated in the cases with chronic thyroiditis which appeared familially as an autosomal dominant trait. The examined families were three. Family Ki'.s was previously reported by us[1] as a family of Alport's syndrome with chronic thyroiditis, in which four cases of Alport's syndrome with chronic thyroiditis and two cases with chronic thyroiditis alone were observed in three generations. Family Mu'.s had two cases of chronic thyroiditis and elliptocytosis in two generations. Family Mi'.s was also previously reported by us[2] as a family of familial latent autoimmune thyroiditis, in which six cases with no clinical symptom except for having serum antithyroid antibodies were observed in three generations.

Chromosome analysis was performed for cultured leukocytes by the ordinary Giemsa staining and G-banding techniques. At least two cases with serum antithyroid antibodies from each of these families were examined in the study.

The results were as follows. In the first family (Ki'.s), a 64 year-old female of Alport's syndrome with chronic thyroiditis revealed to have karyotypes of about 10 percent trisomy mosaic picture of 46, XX/47, XX, +G, and her grandson, a 19 year-old male with chronic thyroiditis and preclinical stage of Alport's syndrome showed also 10 percent trisomy mosaic picture of 46, XY/47, XY, +G.[3] In the second family (Mu'.s), a 50 year-old female and her daughter, a 23 year-old female, who had the chronic thyroiditis and elliptocytosis, showed similarly about 4 percent trisomy mosaic picture of 46, XX/47, XX, +D respectively. In the third family (Mi'.s), a 61 year-old male, who had serum antithyroid antibodies and chronic thyroiditis confirmed histologically, showed karyotypes of about 10 percent trisomy mosaic picture of 46, XY/47, XY, +E. But his daughter, a 23 year-old female with chronic thyroiditis did not show the trisomy.

Thus, normal/trisomy mosaicism was demonstrated in familial chronic thyroiditis of various kinds, in both of examined two cases in two families and one of two in one family. The trisomy found in these cases were different such as G, D or E for the families, but same in the same family.

The results are noteworthy in reference to the fact that there is a high incidence of chronic thyroiditis in the patients of Down's syndrome and their mothers.

Reference: 1) Miyoshi, K. *et al.* 1975. Antithyroid antibodies in Alport's syndrome. *Lancet* **II**: 480-482, 2) Miyoshi, K. *et al.* 1976. Familial latent autoimmune thyroiditis. *Jap. J. Allerg.* **25**: 417. 3) Miyoshi, K. *et al.* 1976. Trisomy G mosaicism in Alport's syndrome (hereditary nephritis with deafness). *Jap. J. Human Gent.* **20**: 266-267.

〔**質問**〕 **山県猛司** (国立岡山病院・小児科)：家族性慢性甲状腺炎を伴わないAlport病についての染色体分析をされたことがあるか.

〔**答**〕 **河内康憲**：Alport 症候群として染色体検索を行なったのは，この一家系だけである.

〔**質問**〕 **塩野　寛** (国立西札幌病院)：抗甲状腺抗体が高いことがどのように染色体異常に関与しているのか.

〔**答**〕 **山野利尚**：本報は，家族性慢性甲状腺炎に染色体異常がみられたということである. Fialkowが慢性甲状腺炎が染色体異常を起すといっているのは Down 症という病態についての検討の結果であるので，われわれの内容とは異なる. 家族性慢性甲状腺炎にトリソミーモザイクのみられる意味については，現在考えているところである.

52. **Masayasu HAYASHI** (Dept. Ophthal., Juntendo Univ., Tokyo) **and S. De BIE** (Dept. Med. Genet., Gent Univ., Belgium): **The Palmer Axial Triradius Revisited.**

Although usually only one axial triradius can be seen on the human palm, occasionally two or more are present. In earlier publications, all the axial triradii are mentioned in the palm formula, but for tracing main-line T the most *proximal* one is taken. After the introduction of the maximal atd angle, the most *distal* axial triradius is generally used. However, David (1971; 1972) showed that the frequency distribution of the corrected atd angle is normal, when the most proximal axial triradius is used, and he suggests that in presence of multiple axial triradii the most distal one is only a manifestation of some hypothenar pattern.

We think that the most proximal triradius should be used. Indeed, the analysis of the position of the axial triradius by breadth ratio (Hayashi and De Bie, 1975) in a Belgian control population revealed a more irregular distribution for the most distal than for the most proximal triradius. On 126 palms with more than one axial triradius we find that the frequency distribution of the breadth ratio for the most proximal axial triradius is very similar to that of the whole sample; the distribution of the most distal one is quite different. Moreover, the curve of the most distal triradius is bimodal. These distributions allow to classify the triradius easily in t, t′ and t″.

If the human palm with a radial arch with borderline triradius on the hypothenar and without axial triradius is presumed to be the most elementary form, three points, which are more predisposed to develop into a triradius can be imagined on

this pattern: a distal, a middle and a proximal one. Usually only a proximal triradius is formed, the borderline triradius disappears and the hypothenar becomes an open field.

In conclusion, we think: 1. that when more than one triradius is present, the distal one(s) can not be considered as the axial triradius. 2. that three types which can be distinguished from the frequency distribution corresponds to these three different origins of palmer triradii.

53. **Kazuhiko ABE and Noboru ODA** (Dept. Psychiat., Osaka City Univ., Osaka): **Prevalence of Childhood Speech Retardation in Parents of Children with Motor Dysphasia.**

In order to examine genetic factors in developmental motor dysphasia, children belonging to the following category were selected from those whose parents' childhood information including speech development could be obtained from the paternal and maternal grandmothers.

I) Started to talk later than 24 months of age, but no significant retardation at 36 months.

II) Could speak words intelligible to adults but could not make a sentence at 36 months.

III) Could not yet speak words intelligible to adults (other than the mother) at 36 months.

All of these children had been examined within 15 days of their third birthday at Abeno Health Center and had been found to be able to understand spoken words. As controls, 198 children who had never shown speech retardation were selected.

Table 1. Childhood speech retardation in the parents of children with motor dysphasia and of the controls.

Childhood speech retardation	Group			Controls
	I	II	III	
in one or both of the parents	19 (37%)	7 (30%)	8 (30%)	46 (23%)
in neither of the parents	32	16	19	152
Total	51	23	27	198

Prevalences of speech retardation in the parents of the above Group I, II, III and the control children are shown in Table 1. It is significantly higher in dysphasic children than in the controls, and appears higher in children with the transitory type (Group I) than in other groups of dysphasic children but the latter

difference is not statistically significant.

Further, the prevalence is highest in the fathers of dysphasic girls and lowest in the mothers of dysphasic boys, a finding suggestive of a polygenic inheritance with a lower threshold of manifestation for males, although no definite conclusion can be drawn on this point, due to the small size of the sample (Table 2).

Table 2. Prevalence of childhood speech retardation in the fathers as compared with the mothers of children with motor dysphasia.

Parents of	Prevalence in	
	Fathers	Mothers
70 boys	15 (21±5%)	10 (14±3%)
33 girls	8 (24±7%)	7 (21±7%)

Table 3. Reports of 100 grandmothers on two occasions on the same offspring, the proband's parent. The plus sign (+) shows the grandmothers positive answer with regard to speech retardation.

	Earlier answer	
	+	−
Recent answer	+5	5
	−6	84
Total	11	89

As an attempt to assess the reliability of the data reported by the grandmothers, the concordance of their answers obtained on two different occasion, separated on the average by an interval of 3 years, were examined as follows: 50 three-year-old children whose elder siblings had been also examined at the age of three years in the same well child clinic were selected. On the occasion when the elder siblings were examined the respective paternal and maternal grandmothers filled in questionnaires on the parents. These questionnaires ("earlier answers" in Table 3) are compared with those recently obtained when the younger siblings were examined. The concordance rate with regard to speech retardation is found to be 89% (Table 3).

54. **Yasutsune SUZUKI, Seiji SAITO** (Dept. Otolaryngol., Keio Univ., Tokyo), **Ryo WAKABAYASHI** (Dept. Pediat., Keio Univ., Tokyo) **and Soichiro ASANAMI** (Dept. Dent., Keio Univ., Tokyo): **II B-25 Mohr Syndrome (OFD II).**

Mohr first reported in 1941 that Mohr syndrome (oral-facial-digital syndrome II; O.F.D. II) is a hereditary disease in which abnormalities appear in the hands, oral cavity, nerves or muscles in four men in a family. After that, Claussen reported in 1946 that the syndrome is a inferior heredity. Rimoin and Edgerton recommended in 1967 that the syndrome is called as O.F.D. II classified from O.F.D. There occur malformations in the face, the bottom of the oral cavity or the tongue. Dysacousia in the sound conduction is sometimes associated with polydactyly in patients with this syndrome. Other malformations sometimes occur. They occur as an inferior heredity.

Case: F.K., a 4-month-year-old male. Date of First Diagnosis: February 13, 1976. Chief Complaint: Narsh and poor increase in the body weight. Clinical Course: There were no abnormalities in the pregnancy and delivery. He had harsh, hyperventilation and inspiratory dyspnea at birth. When he was admitted to a certain hospital from October 31 to November 19, he was diagnosed as "trasient polypnea" by the detailed examination. His clinical course was observed. But he visited our hospital with request of his reexamination because the above-mentioned symptoms continued. There are verruciform eruptions in the bottom of the oral cavity and polydactyly as objective symptoms. He has complications of hypertelorism and lobulated tongue. There are gothic palate in the oral cavity and hypoplasia in the mandible (the mentum goes back from the lateral view). From the acoustic reaction of brain-stem, the condition of hearing is 45 db in the air conduction and 35 db in the bone conduction. He has moderate disturbance of hearing, and is strongly suspected of having the disturbance in the sound conduction. There is no abnormality in euchromosomes. These findings showed that he has Mohr syndrome (oral-facial-digital syndrome II).

55. **Naoko SASAKI, Hisaomi KAWAI, Yoshiaki TADA, Mitsuharu HIASA, Masaru IWASA, Kanae KUSAKA and Kazuo MIYOSHI** (Dept. Int. Med., Tokushima Univ., Tokushima): **Duchenne Type of Progressive Muscular Dystrophy Associated with Color Blindness.**

Tow cases of Duchenne type of progressive muscular dystrophy (DMD) from two families and one case of childhood muscular dystrophy from one family, combining color blindness respectively, were reported.

Case 1 (Ya.'s), a 14 year-old boy with DMD and deuteranomalia had gait

disturbance at 1.5 years of age and inability of gait by the age of 8. Muscular atrophy was present in the muscular groups of the trunk and the pelvic girdle with pseudohypertrophy of the gastrocnemius. The serum creatine kinase activity was 456 units (the normal value is below 25). His two sibships of 18 and 20 years of age had only color blindness. Their mother was a female gene carrier of DMD with a slight elevation of serum creatine kinase activity to 31 units and had color blindness. Three of five male sibships of the mother died of DMD, whose color blindness was not known. The rest two were healthy and had only color blindness. In this family, the mother's chromosomes $X^{cd}X^{c}$ (c: color blindness, d: DMD) were considered to be separately transmitted to the 3 male offsprings. Case 2 (Ni.'s), a 11 year-old boy with DMD and deuteranormalia had gait disturbance at the age of 1.5 years and developed inability of gait by the age of 10 with muscular atrophy in the trunk and the proximity of the extremities. The serum creatine kinase activity was 715 units. Only color blindness was present in his elder brother and a cousin of the maternal side. The mother was a female gene carrier of DMD with an elevation of serum creatine kinase activity to 35 units and had color blindness. In this family, the mother's chromosomes $X^{cd}X^{c}$ was considered to be transmitted also separately to the boys. Case 3 (Ma.'s), a 11 year-old boy with childhood muscular dystrophy and deuteranopia, developed waddle gait by the age of 5 with muscular atrophy in the trunk and the proximity of the extremities. The serum creatine kinase activity was 52 units. In this family, on his paternal side there was a second cousin, whose children of 14 year-old girl and 10 year-old boy had childhood muscular dystrophy with serum creatine kinase activity 329 units and 783 units, respectively. The initial gait disturbance of these two cases was at the age of 1 and 1.5 years respectively, developing the same muscular atrophy of the trunk and the proximal muscles of the extremities. Although they were unable to be differentiated from DMD by the clinical symptoms and course, they were the cases of autosomal recessive genotype of PMD (malignant limb-girdle type)[1]. The genotype of these three cases in this family was $d'd'X^{c}Y$, $d'd'XX$ or $d'd'XY$ (c: color blindness, d': malignant limb-girdle type of PMD) respectively.

Up to present, the report of DMD with color blindness is scanty. There is no other report in Japan. Only 10 families including our 2 families have been reported. Of these, only 3 families reported by Philip *et al.*[2] and Zatz *et al.*[3] are available for the precise genetic study, having definite DMD cases with or without color blindness. In these families, DMD appeared combined with color blindness in 9, muscular dystrophy in 6, color blindness in 7, and normal in 16. Meanwhile, 3 family cases of Becker type PMD (BMD) with color blindness have been reported

by Emery *et al.*[4] and Skinner *et al.*,[5] in which BMD and color blindness appeared combined in 18, muscular dystrophy in 10, color blindness in 10, and normal in 27. The precise genetic calculation on the loci of the genes of both DMD or BMD and color blindness should be done based on these data and further cases should be found hereafter.

References: 1) Miyoshi, K. *et al.* 1966. *Clin. Neurol.* **6**: 491. 2) Philip, U. *et al.* 1956. *Ann. Hum. Genet.* **21**: 155. 3) Zatz, M. *et al.* 1974. *J. Med. Genet.* **11**: 321. 4) Emery, A.E.H. *et al.* 1969. *Ann. Hum. Genet.* **32**: 261. 5) Skinner, R. *et al.* 1974. *J. Med. Genet.* **11**: 317.

〔**質問**〕 **田中克己**(東医歯大・人類遺伝)：第1家系の発端者の母の兄弟で色盲と筋ジストロフィーが分離しており，連鎖のテストが可能かと思われる．

〔**答**〕 **佐々木尚子**：発端者の母親の兄弟の中で，3人の DMD については，すでに死亡のため，color blindness の検索はできていない．このため，DMD と color blindness が separate しているかどうかについてはわからない．

56. **Fumio HIGUCHI, Kotaro FURUYA, Keisuke ONCHI and Masamitsu TSUCHIYA** (Dept. Orth., Tokyo Med. Dent. Univ., Tokyo): **The Inheritance of Congenital Dislocation of the Hip in Japan.**

The disease of the congenital dislocation of the hip has long been recognized since the Greek era, but its etiology is still unknown and it is also doubtful whether it is really congenital or not. Quite a number of theories have been published as to its patho-genesis, none of which are always correct. It seems certain that the congenital hip dislocation is completed not only by genetic, but environmental factors. As to its genes, somebody said dominant and another recessive, but it is considered polygenic at present. In 1971, Woolf presumed the heritability of the congenital hip dislocation 0.82 and 0.58 in males and females, respectively, based upon Falconer's threshold theory. To know these values in Japan, we investigated the family history and birth history of the 103 probands with the congenital hip dislocation who visited our clinic from 1972 to 1975. There were 98 females and 5 males. On the other hand, our data on the incidence of the congenital hip dislocation in general population showed 0.1% in males and 0.6% in females, based upon click test to the 4 mouth babies. Yamada concluded that the male and female incidence was 0.4% and 1.35% respectively from his new born baby check. The difference between his data and ours is not so small and it might be the reason that his checked cases contained not only pure dislocations, but spontaneously healed cases or babies with dysplastic acetabula. Thinking of threshold, Yamada's method is preferable, therefore, we used mean values as its incidence. Since male probands were too few to analyse, we used only female probands. Four sisters of 47 siblings (8.5%) of them were affected with the congenital dis-

location of the hip. From these data the heritability was presumed 0.67. It seems a little higher than that of Woolf, but these materials are too small for analysis, so that we are planning to collect more data and to report on a detailed analysis separately in male and female cases.

57. **Yukie IKEDA, Makoto HIGURASHI, Munehiro HIRAYAMA** (Dept. Maternal and Child Health, Univ. Tokyo, Tokyo), **Norihiko ISHIKAWA** (Dept. Pediat., Univ. Tokyo, Tokyo) **and Hiroki HOSHINO** (Dept. Pediat., Kyorin Univ., Tokyo): **A Longitudinal Study on the Anthropometric Measurements of Stature, Sitting Height, Lower Limb Length and Upper Limb Length in Japanese Children with Down's Syndrome.**

It has been said that the physical growth of children with Down's syndrome shows anatomic deviations from normal children. This study was designed to clarify longitudinally the growth patterns of stature, sitting height, lower limb length and upper limb length in infants with Down's syndrome and the change in size of the lower and upper limb length relative to stature during first four years of life.

Subjects were 52 children with Down's syndrome (27 boys, 25 girls) and 98 normal controls (50 boys, 48 girls). All cases with Down's syndrome were regular 21 trisomic except one boy and one girl with the D/G translocation type. All nude subjects were measured by Martin's meathod. Measurements of all the subjects were repeated every 3 months from birth to 12 months of age, and every 6 months after 12 months of age. Anthropometric measurements were made on stature, sitting height, lower limb length and upper limb length. The longitudinal data were collected over a period of three years on both groups.

The stature, the lower limb length and the upper limb length in the children with Down's syndrome were significantly shorter than those in normal controls. On the other hand, the differences of sitting height between Down's syndrome and normal controls were not significant. From our observations it can be concluded that the shortness of stature in children with Down's syndrome is mainly due to failure of their lower limb length.

In the relative lower limb length (lower limb length/stature$\times$100) and the relative upper limb length (upper limb length/stature$\times$100), the indices of the children with Down's syndrome were smaller than normal controls. Thus Down's children show an infantile proportion.

The trends were that the monthly incremental gains of children with Down's syndrome in stature, lower and upper limb length were smaller than those of normal controls. It suggests that the reduced stature observed in the children

with Down's syndrome results from a severe reductions in the rate of growth of lower limb length in the early years of life.

58. **Meisho KO, Toru NAKAMURA, Hideto FUJITA, Masakuni SUZUKI** (Dept. Obst. Gynec., Tohoku Univ., Sendai) **and Katsuaki SAGISAKA** (Dept. Obst. Gynec., Yamagata City Hospital Saiseikan, Yamagata): **Clinical Study in Primary Amenorrhea.**

The clinical study of 19 patients with primary amenorrhea visited our O.P.D. during the recent two years is presented. The chromosomal analysis revealed Turner's syndrome in 3 cases, testicular feminization in 2 cases and primary amenorrhea with 46, XX karyotype including 3 cases of atresia vagina in 14 cases. Amenorrhea was due to chromosome anomaly in the Turner's syndrome, hormonal anomaly in the testicular feminization and malformation in the atresia vagina. Besides chromosomal analysis, somatometria, examinations of bone age, dermatoglyphics, secondary sexual characteristics and genital condition, and I.Q. test were carried out.

The purpose of this study is to establish a standard criteria for the differential diagnosis of the mosaic case from the primary amenorrhea, if such cases exist. From the analysis, we found that there may be some mosaic anomalies in the primary amenorrhea with 46, XX karyotype, and some relationships between Turner's syndrome and primary amenorrhea with 46, XX karyotype were suggested. Though the cases examined were scarce and the gonadal tissue, skin and bone marrow have not yet been examined, the possibility of mosaic status cannot be excluded.

59. **松永 英** (国立遺伝研): **網膜芽細胞腫の再発危険率について.** Ei MATSUNAGA (Nat. Inst. Genet., Mishima): **On the Recurrence Risks of Retinoblastoma in Relatives of the Patients.**

網膜芽細胞腫の大多数は孤発性であるが，一部は家族性に発生する．家族例の主体は，健康な保因者を親に持つ同胞内多発例であったが，最近は治療した孤発例の親から子に遺伝する例がふえており，それだけに遺伝相談の必要性が高まってきた．

ところで網膜芽細胞腫の再発危険率は，これまで Vogel (1967) や Fiore (1976) らによって，優性遺伝子の浸透率を一律に 80% とみなして計算されてきた．しかし，演者が家族性症例を分析した結果，優性遺伝子を受けついだ子における浸透率は，保因者である親の表現度に応じて変異することが判明した．すなわち，子の再発危険率は，親が両眼罹患のときは 50%，片眼のときは約 45%，無症状のときは約 30% となる．一方，追跡調査の結果，孤発性両眼例のすべては遺伝性とみなされ，その約 8 %は（健康な）保因者の親からの遺伝で，残りは新生突然変異によると考えられる．また，孤発性片眼例の約 95% は非遺伝性で，残り 5 %が遺伝性とみなされるが，後者の内訳（新生突然変

異と保因者からの遺伝）は不明である．

以上のパラメーターに基づいて，患者の血族に対する再発危険率を推定することができる．例えば，孤発性片眼例の子または同胞の再発危険率は約2％，孤発性両眼例の同胞のそれは約3％となる．なお，遺伝相談でもっとも重要なのは，発端者が孤発性片眼例の場合にそれが遺伝性か非遺伝性かの鑑別である．もし腫瘍の多巣性，13番染色体の長腕の一部欠失，骨肉腫などの二次性腫瘍の発生，親の眼底の陳旧瘢痕のうち，いずれか一つが認められれば遺伝性の診断が確定する．しかしこれらの所見が認められることはむしろ稀であるところに，鑑別診断に残された問題がある．

〔**質問**〕 **浜口秀夫**（筑波大・医・人類遺伝）：眼球摘出を受けたために長期生存している遺伝性網膜芽細胞腫の患者で，二次性腫瘍を発生した患者はどれくらいいたか．その腫瘍の種類とその腫瘍は網膜芽細胞腫遺伝子によって発生してきたと考えられるかどうかもあわせ教えていただきたい．

〔**答**〕 **松永　英**：自験例で1例に二次性腫瘍の発生をみた．これは両眼性孤発の母（発端者）に生まれた娘で，3歳時に左眼に発病して眼球を摘出されたが，右眼にも網膜芽細胞腫が発生し，コバルトの照射を受けた．本例は術後5年以上を健康に経過したが，12歳時に右上顎骨の骨肉腫を発生し死亡した．文献的にみると，二次性腫瘍の大多数は骨肉腫で，これは網膜芽細胞腫の優性遺伝子の多面効果とみなされる．

60. **Kiyotaro KONDO** (Dept. Neurol., Brain Res. Inst., Niigata Univ., Niigata): **Multifactorial Causation of Adult Diseases; Computer Simulation and Surveys of Parkinson's Disease.**

The liability/threshold hypothesis has provided a model for some congenital diseases. For adult diseases, however, there are uncertainties how delayed onset may be explained in term of multifactorial gene-environment interactions, although cumulated environmental effect is probably important in some disorders like diabetes mellitus. The objective of the present study is to compare results of a simulation with observed features of Parkinson's disease to evaluate whether age factor in the gene action, rather than cumulated environmental effect, may underlie its onset in the elderly age.

A hypothetical multifactorial disease was produced in a computer. 500 each of families were produced for different conditions regarding gene frequencies and weights of the environmental factors. For a given threshold, frequencies of the disease were calculated in general panmictic population and among children having no, one or two affected parents. Assuming that each allele has its own period of action during life time, the age of onset curves were also formulated. Simulated patterns of the hypothetical disease were compatible with those expected theoretically (Carter, 1961, 1969). Age distributions at onset were increasing with age, with a drop in the extreme elderly group.

Frequencies and the family patterns of Parkinson's disease were surveyed in Niigata, Japan, Rochester, Minnesota, USA, and Sweden. Prevalence rate was low

in Niigata where the sib recurrence rate was also low. Estimated heritability was about 80% in all areas, and the family patterns were compatible with those in a multifactorial inheritance (Kondo *et al.*, 1973). The age-specific incidence rates were increasing with age, but declining in 70's and over.

It is likely, at least in some adult diseases, that age factor in gene actions is the major mechanism of delayed onset, particularly in diseases with high heritability and those showing no association with extrinsic factors.

〔**質問**〕 **松永 英**（国立遺伝研）：Parkinson 病の一般集団における有病率は，日本では欧米よりもずっと低く，かつ遺伝率も日本では低いように見える．もしそうであれば，日本では Parkinson 病の遺伝子頻度そのものが，欧米よりも低いことになり，興味深い．ただし Falconer の方法による遺伝率の推定値は実際の値よりも低く出るから，この点の補正を加えれば，おそらく遺伝率は 10% くらい高くなるだろう．

〔**答**〕 **近藤喜代太郎**：遺伝率の地域差は，データの質に地域差があるのでなんともいえない．

61. **平山清武・田中 洋・外間登美子**（琉大・小児科）**・寺脇 保・荒田弘道・郷緒良三・井手節雄・池田琢哉**（鹿大・小児科）：**沖縄における人類遺伝学的研究**．Kiyotake HIRAYAMA, Hiroshi TANAKA, Tomiko HOKAMA (Dept. Pediat., Univ. Ryukyu, Okinawa), Tamotsu TERAWAKI, Hiromichi ARATA, Ryozho GOHO, Setsuo IDE and Takuya IKEDA (Dept. Pediat., Univ. Kagoshima, Kagoshima): **Human Genetic Study in Okinawa.**

私どもは多年，南西諸島の人類遺伝学的検討をおこなってきた．今回は沖縄本島の首里（721名），糸満（277 名）の小学生を中心に，あわせて鹿児島市（298 名）の小学生を対象に各種形質について調査した成績を報告した．

1. ABO 血液型：首里，糸満では九州平均に比較しA型が多く（41.8%，53.6%），B型が少ない（16.3%, 14.1%）．これに対して鹿児島市では屋久島，九州平均に類似している（A38.9%，B22.8%）．

2. PTC 味盲：首里（14.1%），糸満（17.8%）は白人より低く，鹿児島市は 12.1% であった．

3. 耳垢型 wet 頻度：首里（54.5%），糸満（59.8%）とも高く，鹿児島市（22.5%）は南西諸島と日本平均の中間値である．

4. 二重眼瞼頻度：首里（76.1%），糸満（78.3%）は高く，鹿児島市（54%）は南西諸島より低い．

5. 蒙古ひだ陰性：首里（56%），糸満（61.6%）は屋久島（32%）にくらべ高く，鹿児島市は36.9%であった．

6. 指紋各型頻度：首里は A 2.4, R2.4, U 50.0, W 45.2%，糸満はA 3.2, R 2.1, U 55.9, W38.9%，鹿児島市はA2.6, R3.1, U47.6, W46.8%で，各種指数を算出すると前二者は南太平洋グループに近い値を示した．

62. **Masakatsu HOMMA, Bunsaku NAGAI, Takashi MITSUYAMA, Yogo OKA, Shinichiro ARASHIMA** (Dept. Pediat., Hokkaido Univ., Sapporo), **Michiya ANAKURA, Haruo NANBU** (Nakanoshima-Chuo Hosp., Sapporo) **and Ichiro MATSUDA** (Dept. Pediat., Kumamoto Univ., Kumamoto): **A Family of Fucosidosis.**

Fucosidosis is a rare inborn error of metabolism due to the deficiency of α-L-fucosidase. Clinical manifestations are severe progressive cerebral degeneration, Hurler-like appearance and skeletal changes. Since it was first reported by Durand in 1966, there have been twelve cases with fucosidosis. We report here clinical and biochemical findings of three new cases in a family.

Case 1: 4 1/6 year girl. She complained of progressive psychomotor retardation. She was diagnosied on the basis of characteristic features, beaking of vertebral bodies and low fucosidase activity in leukocytes. She had frequent episodes of pneumonia, and died at 5 2/3 years old.

Case 2 and 3: 1 1/3 year old twins, sisters of case 1. They had recurrent upper respiratory tract infection and progressive psychomotor retardation, which began at birth.

In both cases, vacuolized lymphocytes were found in a few percent in the peripheral blood smear, but the EEG showed normal. Activity of lysosomal enzymes in their leukocytes was deficient.

〔**質問**〕 **北川照男**（日大・小児）：1) 尿中の fucose 含有多糖体は増量していたか.

2) Fucosidosis の保因者診断において fucosidase 活性を測定する場合，白血球と線維芽細胞のいずれを使用した時に信頼度の高い結果が得られるか.

〔**答**〕 **荒島真一郎**：1) 尿中フコース含有糖脂質，糖タンパクについては現在神戸大生化学木幡先生に分析を依頼中である.

2) 保因者検索で白血球と皮膚 fibroblast でどちらが有利であるという点については差がなかった.

〔**質問**〕 **柳瀬敏幸**（九大・一内）：この例はスフィンゴリピドーシスでなく，ムコ多糖症でもなく，ムコリピドーシスに属する日本で唯一の報告例とみて注目していたが，これは定型的なフコシドーシスとみてよいか．その理由は，一連のムコリピドーシスは entity の重複がまだ疑われていて，I-cell disease やフコシドーシス，その他のムコリピドーシスとの descrimination がむずかしい場合がありそうに思えるからである.

〔**答**〕 **荒島真一郎**：第1の例は日本ではじめて報告された例である．酵素学的に fucosidase 欠損が証明されているだけでなく，肝生検材料について fucose を多く含んだ糖脂質，糖タンパクの蓄積が認められ，すでに報告している．Fucosidosis の診断は確定したものと考えている.

われわれの3例を含めて，現在まで世界で15例の報告がある.

63. **大柳和彦・十川英明・折居忠夫**（札医大・小児科）：**高オルニチン血症の一例**. Kazuhiko OYANAGI, Hideaki SOGAWA and Tadao ORII (Dept. Pediat., Sapporo Med. College, Sapporo): **A Case of Hyperornithinemia.**

高オルニチン血症は遺伝性のアミノ酸代謝異常症で，現在二つの type のものが知られている．すなわち，1968年 Bickel らにより報告された同胞例で ornithine ketoacid transaminase の部分欠損による本症で，血中アンモニアは常に正常である．一方，1969年 Shih らは高アンモニア血症，ホモシトルリン尿症を伴う高オルニチン血症を報告した．今回私たちは，前者の type と思われる症例を経験したので報告する．

症例15歳男児，主訴は知能障害，肝機能障害である．両親に血族結婚は認めず，家系内に同様の疾患を有するものはない．検査成績では低タンパク血症，軽度の肝機能障害，肝の組織像で線維化が強い，肝硬変への移行像を呈した．血中アンモニア，セルロプラスミン，尿中オロチン酸は常に正常であった．眼科的にも全く正常であった．血清アミノ酸分析ではオルニチンのみの異常高値（160～400 μmole/l）が認められたが，尿中アミノ酸排泄はほぼ正常パターンを示した．患児ならびにその家族に L-オルニチン 100 mg/kg の経口負荷試験を行ったが，患児では負荷後血中オルニチン値の異常高値が持続し，家族では，母親の血中オルニチンの経時的推移で患児と正常者のほぼ中間値を示し，保因者と思われる．従来の報告では常染色体劣性遺伝形式をとると考えられているが，私たちの家系では父親に異常を認めず，伴性劣性遺伝の可能性が示唆された．今後酵素学的検索とともに，さらに広い家族的検索を進めて，本症例の本態および遺伝形式を明らかにするつもりである．

〔質問〕 **北川照男**（日大・小児）：オルニチン負荷試験において，血中オルニチン量は対照より高値を示したにもかかわらず，尿中オルニチン排泄量は増加しなかったと報告したが，その機構をどのように考えているか．

〔質問〕 **荒島真一郎**（北大・小児）：肝障害がある場合，血中オルニチンはどの程度上昇するか．肝障害が原発か，二次的なものか，酵素活性を測定してみなければ確定診断はむずかしいと思われる．

〔答〕 **大柳和彦**：1) 患児で尿中オルニチンの排泄増加がみられなかったのは，腎でほとんど再吸収されたものと推定せざるをえないと思う．御指摘のように小きざみに採尿すれば差が出るかもしれない．

2) 御指摘のように enzyme assay は不可欠で，現在 fibroblast で検討中である．肝障害のためにオルニチンが上昇したとは考えにくく，肝障害時には他のアミノ酸，メチオニン，ロイシン，イソロイシンなどが高値を示すのが一般的と思う．

64. **大村 清・樋上 忍・多田啓也**（大阪市大・小児科）：**白血球による Hurler 症候群，Sheie 症候群，Niemann-Pick 病および Metachromatic Leukodystrophy の患者およびその保因者診断**. Kiyoshi OMURA, Shinobu HIGAMI and Keiya TADA (Dept. Pediat., Osaka City Univ., Osaka): **Diagnosis of Homozygotes and Heterozygotes of Hurler Syndrome, Sheie Syndrome, Niemann-Pick Disease and Metachromatic Leukodystrophy by Leucocyte Enzyme Assay.**

Hurler 症候群2家系，Sheie 症候群2家系において白血球の α-L-iduronidase 活性を測定した．Hurler 症候群の患児では活性は全く認められず，保因者である両親は正常対照のほぼ 1/2 の活性を示した．Sheie 症候群の患児でも著明な活性低下が認められたが，保因者である両親の中には正常の活性を示す例があった．しかし，α-L-iduronidase 活性を β-galactosidase 活性との比として表わ

すことにより，この重複を少なくすることができた．したがって，保因者の診断には，この比を調べるのが最適と考えられた．

Niemann-Pick 病 (Type A) の1家系において，患者およびその両親の白血球 sphingomyelinase 活性を測定した．患児では活性はほとんど認められず，両親は正常対照の父 18.9%，母 36.4%と低値を示した．これは Brady らの報告と一致し，Niemann-Pick 病 (Type A) の診断が白血球で可能であることを示すものであった．

Metachromatic leukodystrophy (late infantile form) の1家系について，3代にわたり12名の白血球 arylsulfatase A 活性を測定し，患者のみならず保因者をも明らかにすることができた．

以上は，mucopolysaccharidosis および lipidosis の診断，特に，その保因者の診断に際して，白血球の酵素測定が非常に有用であることを示すものである．

〔追加〕 **柳瀬敏幸** (九大・一内)：酵素活性の assay による保因者診断の信頼度を知る一つの基準は，ヘテロ接合体と両方のホモ接合の活性測定値に overlap がなく，完全に分離しているかどうかにある．かなりの数の sample について metachromatic leukodystrophy の保因者の arylsulfatase A の活性はよく分離しているようにみえるから，相当信頼がおけるのではないか．

65. **Jun SASAKI, Kiyohide NUNOI, Katsunori SHIBATA, Kotaro YAMAOKA, Takashi IMAMURA and Toshiyuki YANASE** (First Dept. Med., Kyushu Univ., Fukuoka): **A Case of β-Thalassemia Intermedia.**

The propositus was a 31 year old man who was admitted to the Kyushu University Hospital because of progressive general malaise. He has been noted to show moderately severe anemia since childhood, and mild icterus associated with splenomegaly was pointed out 2 years before hospitalization.

Hematological examinations showed the followings: hemoglobin 7.3 g per 100 ml; hematocrit 25%; red cells count 2.5 million per mm^3; MCHC 28.6%; reticulocytes 4.2%; platelets 63,000 per mm^3; white cells 7,425 per mm^3 (differencial count normal), and erythroblasts 8.5 per 100 WBC. Marked aniso-poikilocytosis, target cells, Jolly's bodies and basophilic stippling were noted in the red cells. Bone marrow examination revealed the myeloid erythroid ratio was 85%. Chemical analyses of the serum disclosed the following: total bilirubin 2.8 mg per 100 ml (2.0 mg indirect form); SGOT 125 mU per ml; SGPT 74 mU per ml; LDH 600 mU per ml over (I 57%, II 29%, III 11%, IV 1%, V 2%); serum iron 247 μg per 100 ml; TIBC 269 μg per 100 ml. Erythrocytes enzyme activities were shown to be increased, but no enzyme deficiency was noted. X-ray film of the skull showed "hair-on-end" figure. Ferrokinetics data revealed markedly increased radioactivity over the slpeen, whereas the bone marrow and liver countings were low.

On thin layer starch gel electrophoresis at pH 8.6, no abnormal hemoglobin was noted. Hemoglobin A_2 and F were quantitated to be 6.0% and 4.7% of the total hemoglobin, respectively. Heat stability tests for unstable hemoglobin were negative.

Heinz body formation was not significantly demonstrated. The β to α globin synthesis ratio was calculated to be 0.72 for peripheral blood, and 1.0 for bone marrow cells of the propositus.

Family study revealed that there were 5 other carriers. Among them three members including the propositus have shown more severe hematological abnormalities than other three who showed only mild anemia and red cell morphological changes as seen in usual β-thalassemia heterozygotes.

The findings presented here support the hypothesis that the valiability of thalassemia genes, the phenotypical expression of which might also be modified by some environmental factors and by interactions with other genetic constitutions, although these conditions are yet poorly understood.

66. **Kazuo HIDAKA, Iwao IUCHI, Katsuko YOSHIDA** (Dept. Biochem., Kawasaki Med. Sch., Kurashiki), **Susumu SHIBATA and Satoshi UEDA** (Dept. Int. Med., Kawasaki Med. Sch., Kurashiki): **Identity of Hb Asabara (α 74 Asp→His) with Hb Kurashiki.**

An electrophoretically slow moving abnormal Hb Asabara was detected in heterozygous condition from 45 yr-old male and one of his two children. The carriers have neither clinical nor hematological aberrancies responsible for the abnormal hemoglobin.

The hemolysate was prepared by traditional way and subjected to electrophoresis (pH 8.6) to separate Hb Asabara as an intermediate component between Hb A and Hb A_2. Hb A_2 Asabara was also seen in electrophoregram, where it was placed more cathodally than Hb A_2. Hb Asabara was purified and examined its primary structure. The results were as follows: 1) PCMB starch gel electrophoresis indicated that Hb Asabara has α chain anomaly. 2) The fingerprint map of tryptic peptide of isolated α chain revealed the appearance of a single new abnormal αTp-9 at just below of αTp-6. 3) The fingerprint map of thermolysin digest of extracted abnormal αTp-9 provided ten peptides including two abnormal peptides and all these ten cleavage products were identified as abnormal αTp-9 origin by amino acid analyses and the two abnormal spots had the same amino acid composition (correspond to α73-79 peptide), therefore, seems to make dislocation on the map by one of their constituent, Met residue is oxidised or not. 4) Stepwise splitting of amino acid from the peptide by Edman-Dansylation method clarified finally these peptides have replaced His instead of Asp at position of 74. Hb Asabara is accordingly represented as the formula of α_2(74 Asp→His)β_2 and completely identical with Hb Kurashiki which was reported by us a few months ago. The two families

live in proximity. It seems reasonable to consider the two family member might be the descendants of the same originate, but this kinship is still unclear.

〔質問〕 **浜口秀夫** (筑波大・人類遺伝) : Hb Asabara の含量が 14.4% ということは, Hb Asabara α 遺伝子の作用の発現が一部抑制されているためと考えられるか.

〔答〕 **日高和夫** : 不安定さはほとんど認められないことから, 生合成が抑制されているために, 減少していると思われる.

67. **Iwao IUCHI, Kazuo HIDAKA, Katsuko YOSHIDA, Hiroko TAKEUCHI** (Dept. Biochem., Kawasaki Med. Sch., Kurashiki), **Susumu SHIBATA and Satoshi UEDA** (Dept. Intern. Med., Kawasaki Med. Sch., Kurashiki): **Hb Akita ($\alpha_2{}^{A(2h)}$ $\beta^{M(1h)}$ $\beta^{M(0h)}$, the Abnormal Red Colored Minor Hemoglobin Found in Hb M Akita (≡Hb M Hyde Park) Disease.**

From the oxyhemoglobin type hemolysate of Hb M Akita (≡Hb M Hyde Park) disease, another abnormal Hb (Hb Akita) was eluted as a minor Hb component by electrophoresis (pH 8.6), which was located as an intermediate between Hb A_2 and Hb A+M Akita.

The component (6.8% of total Hb) revealed β chain anomaly by PCMB-starch gel electrophoresis and it was identified as having the same primary structure of Hb M Akita by fingerprintings, namely, it has a residue of Tyr instead of His in position of β chain at No. 92 from the N-terminus.

The discrepancies of the two proteins in physicochemical characters were as follows: 1) the absorption spectra of Hb Akita in deoxy-, oxy-, cyanmet- and azidomet-Hb types were similar to those of Hb A rather than Hb M Akita. The spectra of acid met- and fluoridomet-Hb forms were, however, favourable to Hb M Akita demonstrating both characters of Hb A and Hb M Akita. 2) Hb Akita is more heat unstable than Hb M Akita and was easily susceptible to the denaturation resulting in the tendency toward heme depletion. It was observed that this heme depletion occurred even in the course of pretreatment for various testings, indicating the value of 2, 2-3, or 3 in the heme number of a molecule. 3) The number of titrative SH residue with PCMB was 1.2-1.4, while that of Hb A was exactly 2.0. 4) Titrative reactivity with ligands (CN^-, N_3^-) of met-Hb Akita was similar to Hb A giving one end point, but remarkably differed from Hb M Akita since it gave two end points. 5) Oxygen equilibrium curve of Hb Akita showed a slight but significant left shift, and heme-heme interaction (Hill's n) was 1.80 (Hb A= 2.80, Hb M Akita=1.3-1.4). The effects of Bohr's and 2, 3-DPG were decreased in comparison with Hb A.

From the result described above, it is reasonable to consider that Hb Akita in oxy-Hb from might have a molecular formulae represented as $\alpha_2{}^A(\text{heme-Fe}^{II})_2\beta^M$-

(heme-Fe^{II})β^{M}(no heme), and that chemical valency of heme iron in β^{M}(heme-Fe^{II}) subunit is not III as in Hb M Akita but II, and is reactive with ligands. The possibility of molecular formulae of $\alpha_2{}^{A}$(heme-Fe^{II})$_2\beta^{A}$(heme-Fe^{II})β^{M}(no heme) was denied.

〔**質問**〕 **林　昭**（阪大・3内）：1) Hb Akita は，われわれが見出した Hb M_{HX} と全く同じもので，その性質もまたきわめてよく類似する（Hayashi, A. *et al.*, *Arch. Biochem. Biophys.*, **125**, 895 (1968)）.

2) Hb Akita の異常 β 鎖ヘム鉄が2価である証拠は何か.

〔**答**〕 **井内岩夫**：Hb Akita の β^{M} 鎖ヘム鉄原子価が2価と考える根拠は O_2, BO などの中性 ligand と反応し，β^{M} サブユニットが対応するスペクトルを示すことである．この点についてはさらに EPR, NMR スペクトルなどをとって検討したい.

68. **Masana OGATA, Junko MIZUGAKI, Kazuko UEDA** (Dept. Public Health, Okayama Univ., Okayama) **and Shigeo TAKAHARA** (Dept. E.N.T., Kawasaki Med. Sch., Kurashiki): **Enzyme Activities of Superoxide Dismutase and Glutathione Peroxidase in Acatalasemia Erythrocyte.**

Acatalasemia is a congenital abnormality having a minute amount of catalase in blood. Enzymes other than catalase; superoxide dismutase (SOD) and glutathione peroxidase (GSH-px) are considered to contribute the generation and decomposition of hydrogen peroxide.

In our preliminary report, glutathione peroxidase prevented the methemoglobin formation from oxyhemoglobin by hydrogen peroxide. In this study, comparison of the activities of SOD and GSH-px in normal and acatalasemia erythrocytes were performed. SOD activity in acatalasemia erythrocytes was higher than that in normal control, while GSH-px activity was a little higher but remained within normal limits.

SOD activity assay: Erythrocytes were washed 3 times with saline and hemolyzed with 1.5 vol of deionized water. For direct assay, the hemolysate was diluted 40-folds and for crude SOD extraction, the hemolysate was prepared for the hemoglobin concentration of 10 g/dl. SOD extraction procedure was employed in the method of Winterbourn *et al.* (1975) and the supernatant was diluted 4-folds. SOD activity was measured with the modified method of Beauchamp and Fridovich (1971); xanthine-xanthine oxidase system under the conditions giving a rate of increase of absorbancy of 0.100/min at 560 nm.

GSH-px activity assay: GSH-px activity in erythrocytes was assayed by the method of Paglia and Valentine (1967), except that the incubation was carried out at 25°C.

SOD activity of normal controls indicated 49.1±7.8 in crude extract and 23.5±

6.0 U/mg Hb (m±SD) in hemolysate from human erythrocytes. SOD activity of 5 human acatalasemias was 61.5±7.1 in crude extract and 35.3±3.8 in hemolysate, indicating higher level than that of normal controls. Differences of mean of SOD activity between acatalasemia and normal controls was significant at the 1% level. Acatalasemia also revealed higher SOD activity than normal in the same family of GIO and MIY. In GIO family, activity was 51.8 in normal and it was 70.9 in acatalasemia, and in MIY family, activity was 49.5 in normal and it was 64.5 in acatalasemia. In mouse erythrocytes, crude SOD activities in acatalasemia showed higher values than those in normal. The activity was 64.0±6.9 in acatalasemia, 61.8±13.7 in hypocatalasemia and 54.8±7.9 U/mg Hb (m±SD) in normal. These results suggested that SOD played an important protective action to the superoxide anion in acatalasemia erythrocytes.

GSH-px activity in human acatalasemia erythrocytes was 5.79±2.22 μmoles NADPH/min/g Hb (m±SD), and it was a little higher than that in normal controls (5.22±1.60). In mouse erythrocytes, GSH-px activity of acatalasemia was 58.4±5.6, hypocatalasemia was 75.1±6.6 and normal was 80.4±1.8 μmoles NADPH/min/g Hb.

References: Beauchamp, C. and Fridovich, I. 1971. *Anal. Biochem.* **44**: 267-287. Paglia, D.E. and Valentine, W.N. 1967. *J. Lab. Clin. Med.* **70**: 158-169. Winterbourn, C.C., Hawkins, R.E., Brian, M. and Carrell, R.W. 1975. *J. Lab. Clin. Med.* **85**: 337-341.

〔**質問**〕 **林　昭**(阪大・3内)：1) アカタラセミア患者血球中のメトヘモグロビン含量は如何. 2) もしあまり増量していなければ SOD 活性の増強は極めて合理的な代償作用と考えられる.

〔**答**〕 **緒方正名**：Acatalasemia の血液ではやや高い程度を示していたと思う.

69. **Masana OGATA, Mikiko IKEDA, Keijiro MORITA** (Dept. Public Health, Okayama Univ., Okayama), **Yasuo KURODA** (Dept. E.N.T., Okayama Univ., Okayama) **and Yasuo SUGATA** (Dept. Hygiene, Jichi Med., Tochigi): **Mercury Uptake by *In Vitro* Human Acatalasemia Blood Samples and by Whole Acatalasemia Mice.**

Magos, Sugata and Clarkson (1974) described that red blood cells preliminary incubated with 3-amino-1, 2, 4-triazole (AT) in the presence of methylene blue, one of hydrogen peroxide (H_2O_2) generating system, showed the decrease in catalase activity and in their ability of mercury uptake from air saturated with mercury vapor. So, mercury uptake by *in vitro* human acatalasemia blood samples (acatala. RBC) and by whole acatalasemia mice (acatala. mice) was investigated.

Method: *In vitro* experiment; Acatala. RBC were washed three times with Krebs-Ringer phosphate buffer (KRPB, pH 7.4). Reaction mixtures were prepared containing 3 g/dl or 5 g/dl hemoglobin (Hb), 15 mM glucose to the final volume of 2.0 ml with KRPB and incubated at 37°C for three hours in Warburg flasks with 0.1 ml

of metallic mercury in a side arm and with or without 0.1 ml of 3% H_2O_2 in a center well. After incubation, an aliquot of them (0.1 to 1.0 ml) was digested by allowing to stand at room temperature overnight after adding 1 to 4 ml of 3% $KMnO_4$ and 10 ml of 10 N H_2SO_4. Total mercury content in them was determined by atomic absorption spectrophotometer (Schimadzu UV-201).

In vitro experiment; Acatala. mice (male) were supplied from Feinstein. Four kinds of mice, normal and acatala. treated with (1 g AT in 5 ml of saline/kg) or without (5 ml of saline/kg) AT i.p. were used for mercury vapor exposure. Dish (10 cm in diameter) filled with metallic mercury was placed at the bottom of the desiccater (20 liter in volume) 30 min before exposure. One hour after injection, the cage, in which four kinds of mice were set separately, was placed in the desiccater for 30 min. The concentration of mercury vapor was determined 15 min intervals by Kitagawa mercury vapor detecter and an average concentration of 10 mg/m^3 was calculated. Organs removed were weighed and digested by the method of Kitamura (1972). They were determined as mentioned above.

Results: *in vitro*; Acatala. RBC showed about 95% decrease of normal RBC in their ability of mercury uptake with or without H_2O_2. For an example, acatala. RBC took in 0.3±0.2 ng Hg/mg Hb without H_2O_2 and 1.4±0.3 with H_2O_2, while normal RBC, 5.2±0.5 and 99.9±10.2 respectively. The role the peroxidase will be discussed in the near future.

In vivo; The different distribution of mercury between normal and acatala. mice was observed. Lung mercury content was remarkably decreased in proportion to the decrease in catalase activity, namely, normal>acatala.>normal treated with AT>acatala. treated with AT in descending order. Similar tendency was observed in blood content. In liver content, however, the opposite phenomenon was found, namely, the increase of mercury content in inverse proportion to catalase activity. Further investigation should be required at this point.

As an conclusion, it is demonstrated that catalase, as catalase-H_2O_2 compound I, plays an important role for oxidation of mercury both *in vitro* and *in vivo*.

70. 津田和矩(宮崎医大・二内)・石橋大海・大久保英雄・柴田勝紀・柳瀬敏幸(九大・一内)：**多型性血漿タンパクの代謝 I. α_1-アンチトリプシンの生体内動態について.**
Kazunori TSUDA (2nd Dept. Int. Med., Miyazaki Med. College, Miyazaki), Hiromi ISHIBASHI, Hideo OHKUBO, Katsunori SHIBATA and Toshiyuki YANASE (1st Dept. Int. Med., Kyushu Univ., Fukuoka): **Metabolism of Polymorphic Plasma Proteins I. Survival of α_1-Antitrypsin in Rats.**

目的：α_1-アンチトリプシン（α_1-AT）欠乏症で肺気腫が発症する機序を *in vivo*, すなわちこのタ

ンパクの生理作用発現の機作との関連から明らかにするために，生体内動態，とくに正常肺と実験的炎症（スポンジ肉芽腫）への経時的な集積の様相をしらべた．

方法：^{125}I 標識の α_1-AT の 0.3 mg をラットに静注負荷し，72時間後まで，一定時間後に臓器・組織を十分に灌流し，単位重量当りの臓器中の放射活性を測定して分布量を算出した．

結果：血中の α_1-AT は負荷後は2相性のカーブを示しながら急速に減衰し，血中半減期は約24時間と概算された．

臓器別の分布では，肺に最も高濃度に，かつ長時間にわたって集積し，腎，筋肉がこれに次ぎ，肝と脾では低値に終始した．さらに 組織/血液比（同一時期における血中放射活性濃度に対する臓器中のそれとの比率）でみると，肺への特有な集積性がうかがわれた．なお肺への分布量は6時間で負荷量のほぼ2％と，肝へのそれの3倍以上に達した．これに対してアルブミンでは肺をはじめ各臓器とも，α_1-AT に比べて低値に終始した．

ラットの背部皮下に作製したスポンジ肉芽腫（平均重量 3.8 g）への分布は，6時間ですでに高値を示し，組織/血液比 ではcapusule, exsudate とも全経過を通じて高値が持続し，とくに後者では72時間後まで増加が見られるなど，筋肉に比べて著しい差異がみられ，またアルブミンの場合に比べて明らかに高い集積がみられた．なお，肉芽腫へは負荷量の 2.7% が12時間後に分布した．

さらに臓器，肉芽腫の放射活性を TCA 上清と沈澱に分画測定した結果，肝，脾，腎などの実質臓器では上清分画の比率が大であったのに対し，肺や肉芽腫では48時間後まで低値が持続し，α_1-AT の分解の少ないことが示唆された．

考察：α_1-AT には肺および炎症性肉芽腫への合目的的ともいえる特有な集積性がみられた．このことから肺の炎症部位には，多量の α_1-AT が需要に応じて供給され，炎症反応を調節するが，欠乏症ではこの調節不全のために，酵素作用による組織の崩壊が進行しやすくなるものと推定した．最後に，このような α_1-AT の生体内動態を調節するメカニズムについても考察した．

〔**質問**〕 **浜口秀夫**（筑波大・人類遺伝）：α_1-Antitrypsin が，肺や実験的肉芽腫に高濃度に高分子の状態で分布しているのは，これらの部位に特有の receptor が存在するためか，またはこれらの部位ではこの血清タンパク質の分解が抑制されているためか．

〔**答**〕 **津田和矩**：われわれの最も興味を持っている問題で，御指摘のように，plasma membrane や receptor などとの interaction を予想している．

71. **Shiro MIWA and Koji NAKASHIMA** (3rd Dept. Int. Med., Yamaguchi Univ., Ube): **Frequency and Type of Glucose 6-Phosphate Dehydrogenase Deficiency in Japan.**

The frequency and the type of glucose 6-phosphate dehydrogenase (G6PD) variants among various populations differ significantly according to race and geography. An example is the high frequency of G6PD deficient variant among Negro and Mediterranean populations which has been explained by selection related to the presence of malaria. Among Mongoloid population, only sporadic cases of this enzyme deficiency have been reported in Japan, while in southern Asia, G6PD deficiency is common. It would be useful, therefore, to do a systematic survey for G6PD deficiency in Japanese who have lived in a relatively isolated island

country where malaria is not endemic. In Yamaguchi prefecture, the screening for G6PD deficiency was performed with Beutler's fluorescent method. Six cases with G6PD variant were found in 7,120 Japanese males. In addition to these 6 cases, 5 cases with G6PD deficiency were found through the red cell enzyme assay for the patients either with congenital hemolytic anemia or drug-induced hemolysis. These 11 cases were characterized using the standard methods recommended by WHO scientific group and 6 different variants were discovered among them.

G6PD Tokyo and Tokushima were associated with chronic hemolytic anemia and classified as Class 1, and G6PD Onoda (2 families) and Ogori have had episodes of hemolytic attack and classified as Class 2. G6PD Hofu and Ube (5 families) have never had hemolysis and classified as Class 3. Abnormal biochemical parameters of these variants were as follows: 1) G6PD Tokyo had severe enzyme deficiency (4.4% of the normal), marked heat-instability and slower electrophoretic mobility; 2) G6PD Tokushima was characterized by severe enzyme deficiency (3.0% of the normal), high K_m for NADP, marked heat-instability and one normal main band with two minor bands of faster and slower mobility on electrophoresis; 3) G6PD Onoda had 3.5% of normal activity, low K_m for G6P, moderate heat-instability, high utilization of three substrate analogs, slightly biphasic pH curve and normal electrophoretic mobility; 4) G6PD Ogori had only 3.5% of normal activity but otherwise normal; 5) G6PD Hofu (12.1% of normal activity) was characterized by low K_m for G6P and high utilization of deamino-NADP; 6) G6PD Ube (45% of normal activity) had fast electrophoretic mobility and high K_i for NADPH.

G6PD Tokyo, Tokushima, Hofu and Ube are unique and differentiated from the previously reported variants. G6PD Onoda, however, is similar to G6PD Mediterranean and G6PD deficiency in Japan is estimated to be less than 0.1%, although the frequencies of other orientals are 5.5% in Southern China, 6.0% in Philippine and 5.5% in Taiwan. The differences in the frequency and the type of G6PD variants in southern Asia and Japan suggest that the Japanese may have been isolated geographically, genetically and anthropologically long enough to have developed their own genetic trait in islands without selective pressure of malaria, even though the racial origin of the Japanese is from southern and northern continental Asia. G6PD Onoda and Ogori must be compared with G6PD Mediterranean and G6PD B(−) Chinese respectively using more advanced methods. If they are proved to be identical respectively, then these variants must be inherited with lower frequency because of hemolysis and no positive pressure of malaria even though they are caused by gene flow from the continent or independent mutation in Japan.

〔追加〕 **影岡武士** (放影研)：当研究所にて行った spot screening test では約 1,000 例中 8 例の

variant を検出した．電気泳動的には fast variant 7例，slow variant 1例であった．約450例の電気泳動による screening (pH 7.0) では，3例の variant を認め，fast variant 2例，slow variant 1例を検出した．

72. **Zen-ichi OGITA** (Dept. Biochem. Pathol., Inst. Oriental Medicines, Univ. Toyama, Toyama), **Ken-ichi YAMAMURA** (Dept. Clini. Biochem., Univ. Osaka, Osaka), **and Shiro MIWA** (Dept. Inter. Med., Univ. Yamaguchi, Ube): **Indentification of Hereditary Disorders and Its Heterozygotes Using Micro-Electrophoresis.**

The indentifications of heterozygosity in the hereditary disorders up to now has been achieved by using sera, leucocytes, urine samples and fibroblasts from patients. The recent introduction of human hair follicle which obtained from the scalp, as a specialized diagnostic sample to detect of the heterozygotes which are X-linked hereditary disorders, has resulted in utilization of biochemical testes by an ever-increasing number of the hereditary units [S.M. Gartler *et al.* (1969, 1971), J.L. Goldstein *et al.* (1971)].

Because the human hair follicle which obtained from the scalp, starts from a small number of cells and exhibits a certain degree of clonal growth, it is useful in the detections of X-linked hereditary disorders. Thus, a female heterozygous for an X-linked genes, will be divided into three phenotypic classes of hair follicles: those consisting of cells expressing only the wild type gene, those with cells expressing only the mutant allele, and third class consisting of both kinds of cells.

Rapid phenotypic diagnosis of the heterozygote was carried out by direct enzyme assay in single hair follicles obtained from the scalp without cell culture techniques.

In order to provide suitable methods for more extensive analysis of single hair follicles, we have miniaturized apparatus and improved electrophoretic conditions for the separation of enzyme activities and undenaturated and denaturated proteins with the anionic detergent, SDS (sodium dodecyl sulfate).

The apparatus has been constructed for the slab gel electrophoresis. The gel slab is made between two Kodak glass plate (83×102 mm). The two glass plates are separated by three 0.8 mm (1/32″) thick neoprene rubber shims placed at the two sides (5×95 mm) and bottom (20×73 mm). The empty sandwich is clamped together and is then made liquid-tight by dripping melted 2.0% agar around the outside edges. The best separation of SDS-denaturated proteins is achieved using 20% to 12% acrylamide gel gradients, and the best condition in undenaturated protein is 8% to 4% the gel gradients. Gartler *et al.* (1961, 1971) have shown previously that single hair follicle in G-6-PD heterozygotes may consist of more than two G-6-PD type, thus demonstrating multiple cell origin of the hair follicle.

Single hair follicles (A/B) were dissected into, bulbs, and outer root sheaths, and separated for G-6-PD type, and for SDS-proteins by the electrophoresis. The zymograms show a marked similarity between the G-6-PD types of the outer sheath and bulb for individual hairs. However, the SDS-protein patterns show a extreme difference between outer sheath and bulb. Using the same technique it was found that a genotype of autosomal hereditary disorders could also be identified in these samples.

73. **Tomotaka SHINODA** (Dept. Chem., Tokyo Metropol. Univ., Tokyo) **and Ken NOZAWA** (Kyoto Univ. Primate Inst., Inuyama): **Variations in Tissue Enzymes in Primates.**

By means of horizontal gel electrophoresis and histochemical staining techniques, phenotypes were analyzed for a total of 25 arbitrarily selected enzymes extracted from tissue specimens of mainly *Macaca fuscata*, with 0.05 M Tris-EDTA-Triton X-100-2ME, containing 0.25 M sucrose, pH 7.0. Enzymes tested in this study included several groups such as oxidases, esterases, dehydrogenases, mutases, reductases, kinases, transferases, *etc.* Of 29 different loci tested, 4 were found to be polymorphic. Thus, the proportion of polymorphic loci in the sample will be roughly 0.14. The value seems somewhat lower than that obtained for man (0.20, Shinoda, 1975). Since the present data are based on a limited number of samples, analysis should be made on a larger number of samples before reaching a more relevant value.

74. **Hideo YAMAGUCHI, Yasuto OKUBO, Taiko SENO, Masayoshi TANAKA** (Osaka Red Cross Blood Center, Osaka), **Yuji ARAKI and Masateru NOGUCHI** (Shizuoka Red Cross Blood Center, Shizuoka): **Another Example of the Blood Phenotype Rh_{mod} Occurring in a Japanese Family.**

The propositus was a 32-year-old male donor whose blood was a first classed as Rh_{null} because of the failure of his red cells to react with any of the routine Rh typing sera, such as anti-D, anti-E, anti-e, anti-C and anti-c. However, further examination indicated that the propositus' red cells gave positive agglutination reactions with all the immune sera tested from the homozygous -D-, cD- and Rh_{null} people, as well as with any of the sera of complex specificities such as anti-C+D, anti-E+c and anti-C+e. Fixation-elution tests gave positive results after exposure of the propositus' cells to anti-D and anti-E but not to anti-C. It was noteworthy that the propositus' s and U antigens were suppressed whereas the M and N antigens were found somewhat enhanced. The serum of the pro

positus did not contain any irregular antibodies. The propositus showed no sign of anemia similar to the Rh_{null} disease.

Pedigree studies indicated that the propositus had four sibs, none of whom had the unusual Rh phenotype similar to that of the propositus. As the propositus' mother was typed as R_1R_2, the propositus' phenotype was assumed not to be due to a rare allele of the *Rh* locus but due to a regulator which was independent of the *Rh* locus and could inhibit or suppress the expression of the normal Rh genes in double dose. The parents of the propositus who were first cousins should be heterozygous for the regulator gene.

At any rate, the Rh_{mod} is known to be an extremely rare Rh phenotype. The present family is the 4th Japanese example and not related to any of the Rh_{mod} families so far detected.

75. **Shigenori IKEMOTO, Kiyoshi MINAGUCHI** (Dept. Legal Med., Jichi Med. Sch., Tochigi): **Genetic Polymorphisms of Human Parotid Salivary Proteins (Pa, Pb, Pr, Db and Pm) and Salivary Amylase Isozyme in Japanese Population.**

Phenotypes and gene frequencies of parotid salivary proteins, Pa, Pb, Pr, Db, Pm and salivary amylase isozyme were studied in the Japanese population. The Pa system was examined in 102 individuals and the gene frequency obtained was 0.227 for Pa^+ and 0.773 for Pa^-. In the Pb system, all 103 samples showed Pb 1-1 type and Pb^2 allelic gene was not found. The Pr and Db systems were examined in 102 individuals and the gene frequency was 0.745 for Pr^1, 0.255 for Pr^2, 0.050 for Db^+ and 0.950 for Db^-.

The Pm phenotypes were examined in 195 individuals and the estimated gene frequency was 0.380 for Pm^+ and 0.620 for Pm^-. The Pm saliva protein is a new genetic marker discovered by the authors and found in the parotid saliva. The Amy_1 phenotypes were examined in 150 individuals and the gene frequency of $Amy_1{}^v$ was 0.010.

Frequencies of Pa, Pb, Pr, Db and Amy_1 systems were compared with those in other reports. The gene frequency of Db^+ in Japanese was lower than in Caucasians (0.12), Negroes (0.56) and Chinese (0.07), while frequencies of Pa^+ and Pb^1 in Japanese were higher than in Caucasins ($Pa^+=0.21$, $Pb^1=0.995$) and Negroes ($Pa^+=0.14$, $Pb^1=0.84$). Frequencies of Pr^1 and $Amy_1{}^v$ in Japanese were somewhat higher than in Caucasians ($Pr^1=0.73$, $Amy_1{}^v=0.005$) but lower than in Negroes ($Pr^1=0.80$, $Amy_1{}^v=0.039$). For the Pm system, comparison with other racial groups has not been carried out.

〔質問〕 **尾本恵市**(東大・人類)：あるシステムの表現型と別のシステムの表現型との間にアソシエィションの見られたものはなかったか.

〔質問〕 **古川 研**(群大・法医)：どのシステムにおいて唾液を濃縮して電気泳動しなければ検出しえないか.

〔答〕 **池本卯典**：Pa, Pb, Pm 表現型相互間には関連は認められない. ただし, Pa と Pr, Pa と Db には相関があると Friedman は説明している. 日本人における調査においても同様である.

Pa, Pb, Pr, Pm, Db システムの検出に当っては, 耳下腺唾液を 5～10 倍に濃縮する必要がある. Amy^1 システムは全唾液を用いる.

76. **Ken FURUKAWA, Keiko SEKI and Shin YAZAWA** (Dept. Legal Med., Gunma Univ., Maebashi): **Water Soluble Antigenic Substance Associated with Blood Group Secretor Types.**

Two separate precipitating antibodies specific for human H substance from blood group secretor types were found in eel (*Anguilla japonica*) sera by Ouchterlony gel diffusion technique. They were designated provisionally to anti-He and anti-Se. Anti-He precipitin reacted well with purified H substances from human and hog gastric linings and human ovarian cyst fluid, while it hardly reacted with human saliva and H substances from human small intestine and meconium. Anti-Se precipitin reacted well with human secretor saliva and H substances but it failed to react with hog H substances. Anti-H and anti-Se precipitinsin eel serum were separated by gel filtration on Sephadex G-200 or L-fucose starch gel affinity chromatography. Anti-He active fraction strongly agglutinated group O red cells, and the agglutinating activity against group O red cells and the precipitating activity against water soluble H substance were inhibited specifically by L-fucose and 2′-fucosyllactose from human milk. The H activities of group O red cells and H substance were destroyed by the action of α-(1→2)-fucosidase from *Bacillus fulminans*. Anti-Se active fraction did not agglutinate group O red cells, and anti-Se precipitin could not be absorbed by group O red cells. The precipitation of H substance by anti-Se could be inhibited by any of the simple sugars which are components of the H substance, *i.e.*, L-fucose, D-galactose, *N*-acetyl-D-glucosamine, and *N*-acetyl-D-galactosamine and by any of α-(1→2)-fucosyl oligosaccharides from human milk. The Se activity of H substance was destroyed by glycosidase preparation of *Clostridium tertium* H, Le^a. α-(1→2)-Fucosidase from *Bac. fulminans* did not affect the Se activity.

The results indicate that the Se antigen found in H substance has different specificity from H antigen which is determined by α-(1→2)-fucosyl residue and the Se antigens exist in water soluble H substances while they does not distribute on red cell surface. It is probable that the production of Se antigen is controlled by

secretor gene.

77. **Hisao TAKIZAWA** (Second Medico-Legal Sec., National Res., Inst., Police Science, Tokyo): **Blood Group ABH and Lewis Antigenic Activities in Glycolipid and Glycoprotein Fractions Isolated from Human Erythrocytes, Gastric Mucosa and Saliva.**

ABH and Lewis blood group activities in glycolipid and glycoprotein fractions of human erythrocytes, gastric mucosa and saliva were investigated with regard to the secretor and the non-secretor.

1) ABH blood group activities of human erythrocytes were detected mainly in glycolipid fraction and partially in glycoprotein fraction. The difference in the blood group activities of these fractions could not be found between the erythrocytes from the secretor and the non-secretor.

2) ABH blood group activities were detected in glycolipid fraction of human gastric mucosa, in equal intensity, from the secretor and the non-secretor. On the other hand, the glycoproteins of gastric mucosa and saliva from the secretor have very strong ABH blood group activities, but these from the non-secretor have not.

3) Lewis blood group activities detected in glycolipid or glycoprotein fractions of erythrocytes, gastric mucosa and saliva were all concerned with the secretor status.

78. **Tadahisa KOGURE and Ken FURUKAWA** (Dept. Legal Med., Gunma Univ., Maebashi): **Enzymatic Conversion of Human Group O Erythrocytes into B Active Cells by α-D-Galactosyltransferases of Urines from Group B and AB Types.**

Fresh urine was immediately dialysed against 40 volumes of 0.01 M Tris-HCl buffer saline (pH 7.2) at 5°C for 24-48 hours. After dialysis, urine was used as the source of α-galactosyltransferase.

α-Galactosyltransferase activity was measured by conversion of red cells. The urine in 200 μl aliquots, was mixed with 20 μl of 1.6 mM UDP-D-galactose, 100 μl of 0.01 M Tris-HCl buffered saline (pH 7.2) containing 0.1 M $MnCl_2$, and 10 μl of 50% O red cell suspension, and the whole was incubated at 37°C 8 hr with occasional shaking. After the incubation, the red cells was washed three times with saline, and a 2% red cell suspension was prepared to determine agglutination titers against the antiserum.

Urines from healthy group B secretor or non-secretor, acting on O red cells in the presence of UDP-D-galactose and $MnCl_2$, each converted them into B active cells, which were agglutinated by anti-B human serum (1 : 512) at the titer of 64

fold, while urines from healthy group AB secretor or non-secretor also converted O red cells into B active cells, which were agglutinated by anti-B human serum (1 : 512) at the titer of 4 to 16 fold. Urine from group O or A donors did not confer B activity on O red cells in the presence of UDP-D-galactose and $MnCl_2$.

The results indicate that the α-galactosyltransferase which participates in the biosynthesis of group B substance is excreted in urine from group B or AB of both secretor and non-secretor types.

α-Galactosyltransferase of urine from group B non-secretor was fractionated by ammonium sulfate fractionation and subsequent column chromatography on Sephadex G-200.

〔**質問**〕 **山本 茂** (科警研)：ヒト尿中から今回分離された α-ガラクトシルトランスフェラーゼ標品の分子サイズは．分子サイズは低いと思うが，ヒトの血清や唾液中の同じ酵素の分子サイズとの間に subunit 的な考えを入れてもよいか．

〔**答**〕 **小暮正久** (群大・法医)：ヒト尿中の α-ガラクトシルトランスフェラーゼ標品について未だ分画が不充分なので，分子サイズについては未定であるが，分子量は10万以下と考えている．尿中のB合成酵素は血清中から腎の糸球体で濾過されてきたものと推定している．subunit 的な考えを入れてよいか不明である．

79. **Takehiko SASAZUKI** (Dept. Biochem. Genet., Med. Res. Inst., Tokyo Med. and Dent. Univ., Tokyo): **HLA Haplotype Differences between Japanese and Caucasians.**

The gene frequencies of HLA-D specificities in Japanese population were surveyed by the method of mixed lymphocyte culture reaction using HLA-D homozygous typing cells, Dw1 through Dw4, and LD HO and LD YT found in the Japanese population. Dw3, which is found at a relatively high frequency in Caucasians, was not seen in the Japanese population. HLA-B8 which is in linkage disequilibrium with Dw3 in Caucasians was not observed in this Japanese population. Thus, one of the most characteristic haplotypes in Caucasians, HLA-B8-Dw3, is absent in the Japanese. Dw1, Dw2 and Dw4 on the other hand, were found to be fairly common antigens in the Japanese population. There are, however, no significant association between these D locus alleles and HLA-B alleles in Japanese in contrast to the presence of linkage disequilibrium between Dw1, Dw2 and Dw4 and particular HLA-B alleles in Caucasians. The new HLA-D specificity, LD HO was seen in Japanese very frequently but was completely absent in Caucasians. LD HO was found to be in strong linkage disequilibrium with Bw35 in Japanese. Bw35-D LD HO is thus a Japanese specific HLA haplotype. The other new specificity LD YT was common in Japanese but was absent in Caucasians. LD YT has strong linkage disequilibrium with Bw22J which is antigenically related to Bw22 but is Japanese

specific. Bw22J-D LD YT is, therefore, also a highly characteristic Japanese haplotype.

It is interesting that the B8-Dw3 haplotype, which is increased in frequency in various autoimmune diseases including Graves' disease, juvenile onset diabetes mellitus, Addison's disease and myasthenia gravis, in Caucasians, is absent from the Japanese population. The incidence of these diseases, in Japanese is comparable to that in Caucasians. It has been reported that Bw35 is significantly increased in frequency in Japanese Graves' patients ant that B8 is absent. D LD HO which is in linkage disequilibrium was increased in frequency in the Japanese patients with Graves' disease. Bw35-D LD HO haplotype in Japanese population is thus comparable to B8-Dw3 haplotype in Caucasians. It is of interest that not only is the frequency of LD HO in Japanese comparable to that of Dw3 in Caucasians, but also the relatively high frequencies of the respective haplotypes Bw35-LD HO and B8-Dw3 are nearly indentical. Furthermore, the delta values for the two haplotypes are very similar. These two haplotypes which are antigenically completely different from each other may have been selected out in these populations because of similar properties. They may share at least one gene closely linked to HLA which is responsible for developing Graves' desease or other autoimmune states (but which might also offer some selective advantage by, for instance, conferring resistance to infection). The nature of such gene(s) is not clear but immune response genes could fulfill these functions. Recent studies in mice have shown that there are complementary immune response genes which appear to function more efficiently in the *cis* position so that particular haplotypes have unique properties of immune responsiveness. If such properties offered a survival advantage, the linkage disequilibrium that is now apparent could be explained.

〔質問〕 **西田尚史**(都立大塚病院)：1座位に20種以上の遺伝子がのるような例が人類に他にあるか.

〔答〕 **笹月健彦**：HLA にみられる高度の多型性は，Bodmer のいうように，pseudoallele ということでも説明できるかもしれない．真に allelic であってももちろん良いし，免疫グロブリンなどにみられる多型性など例は多い.

〔追加〕 **柳瀬敏幸** (九大・一内)：多種類の対立遺伝子の座位は H. Harris や Ford のテキストブックにいくらもその例が示されている．もっとも多いと想定されているのは G-6PD 座位で，100 種類以上推定されている（このなかに pseudoallele や，きわめて密に連鎖しているものがあるかもしれないが)．いま，HLA の研究者は，わが国で次第に増加しつつある．しかし，主として A, B loci を中心にしか分析が進んでおらず，生物学的にも，遺伝学の面からみても，D locus およびその周辺の分析をふくめなくては意義は少ない．今後急速にこの方面の発表は増加し，新知識が展開されると思う．もっとも期待される分野である.

80. **北濱睦夫**(聖マ医大·法医)：**ABO 式血液型遺伝の法則について**. Mutsuo KITAHAMA (Dept. Legal Med., Univ. St. Mariana, Kawasaki): **Review of the Heredity of ABO Blood Groups.**

さきにわれわれは，AmBm 型とO型の夫婦の間から A_1 型1名とO型3名の4人の子供が生れている家系を発見し，発表した．この家系の遺伝関係は *cis*-**AB** とも異なり，現在の遺伝理論では説明がつかない．また，血液型モザイックについても，同様に未だ説明されていない．

そこで，これらの亜型，variant を含めて ABO 式血液型遺伝の法則について再検討を試みてみた．まず，化学的に複雑な構造をもつ血液型物質を，1つの遺伝子の働きで生成されると考えるよりは，いくつかの複数の遺伝子が関与していると考える方が妥当なようである．そこで，これらの遺伝子群を P_1, P_2, P_3……P_0 部分（仮称）に分け，それが P_1, P_2, P_3……P_0 と配列しており，$P_0 \rightarrow P_1$ の方向に共同作業が行われると考えてみた．その結果，A_2 型とは比較的最終の段階で関与する遺伝子部分（P_1 部分）に欠失が起ったものと考えられ，A_x 型は比較的最初の段階（P_x）以上に欠失が起ったと考えられ，それがそのままの状態で遺伝したと思われる．次に，Weiner が変異遺伝子Yをもって説明している Am 型は，遺伝子群の配列に逆位（inversion）が起ったと考えられ，それが次の世代に復帰突然変異（back mutation）様の現象が起って元に戻ったと考えられる．

cis-AB 型は crossing over により A_2B_3 という1つの遺伝群が形成されたために，AB 型とO型の子供が生れたと考えられる．Bombay型は両方の遺伝子群に同時に逆位が起り，そのため血液型の表現がでてこないで，次の世代に復帰突然変異が起ったと考えられる．血液型モザイックは，遺伝子群に切断が起り，その共同作業が断裂したと考えられる．また，さきの AmBm 型の家系は，A遺伝子上に逆位，B遺伝子上に欠失が起ったものと考えられる．

81. **Isamu YONEMURA** (Dept. Legal Med., Shinshu Univ., Matsumoto): **A Model for the ABO Blood Group Genes.**

As to the structure and function of the ABO blood group genes, Noda and Yonemura proposed the model with regard to naturally occurring antibodies in 1975, and afterward I have examined the model and developed this hypothesis suitable for the phenomena concerning ABO blood groups.

The strength of blood group substances among subgroups and variants can not be looked upon as only a quantitative problem. Supposing that the subgroups are typed qualitatively into A_1, A_2 and A_3 and B_1, B_2 and B_3 and the naturally occurring antibodies into α_1, α_2 and α_3 and β_1, β_2 and β_3 and moreover that there exist some genes corresponding respectively with them, these genes will be probably arranged in order $A_1A_2A_3H\beta_3\beta_2\beta_1$ in I^A, $\alpha_1\alpha_2\alpha_3HB_3B_2B_1$ in I^B and $\alpha_1\alpha_2\alpha_3H\beta_3\beta_2\beta_1$ in I^O. Namely, the blood group genes may be multiple genes and the group substance genes may be allelic to the antibody genes. Therefore an H substance gene is considered to be allelic to an anti-H antibody gene (h gene) of the Bombay type. The H substance produced by an *H* gene may be a precursor of A and B substances produced by A and B genes of either *cis* or *trans* position, therefore

only a homologous zygote of the h genes will be Bombay type. The naturally occurring antibodies occur, as Furuhata *et al.* proposed, only when α or β genes are in a homozygous state, but when there are group substance genes corresponding to them, these antibodies may not work at least at about body temperature.

Introducing already known genetical knowledge as the deletion, crossing over (equal and unequal), mutation and gene activation in differrentiation into this fundamental idea, mechanisms of almost all of the things as to the ABO blood groups like subgroups, variants (m-type, x-type and *cis* AB), mosaisisms, irregular antibodies, genetical individualities of the strength of group substances and naturally occurring antibodies, acquired blood group conversion and evolution can be easily illustrated.

〔**質問**〕 **北濱睦夫**(聖マ医大)：1) 自然抗体の免疫発生説も有力な現在，遺伝子によって抗体の発現が制御されていると決めつけるのは妥当ではない．特にβについては問題である．

2) Bombay 型を親にもつ AB 型で抗体が遺伝していない例がある．

〔**答**〕 **米村 勇**：1) 免疫によって自然抗体が発現するという考えは適当ではない（1例を挙げると A_1 型または A_1B 型で非自己である A_2 に対する α_2 をもつものは数%しかなく，さらに自己型質である A_1 に対する α_1 を有する例も知られている)．抗体遺伝子を仮りに α_1, α_2, α_3, β_1, β_2, β_3 と想定すると諸現象の説明にきわめて有利である．

2) 本論でも述べたごとく子供が Hh なる異型接合体であれば正常 AB 型となんら変らない．

82. **宮崎時子**(大阪医大・法医)：**本邦諸地域における免疫グロブリン・アロタイプ (Gm) の分布.** Tokiko MIYAZAKI (Dept. Legal Med., Osaka Med. School, Takatsuki): **The Distribution of Gm Allotypes among the Various Populations in Japan.**

免疫グロブリンのアロタイプである Gm 型は，それが示す二重多型現象によって人類遺伝学の領域において，特異な遺伝標識として役立っている．報告者らはこれまで日本人を中心としたアジア諸地域の集団について，Gm 型および Km 型の分布頻度を調査し，集団間にみられるその遺伝子型の相違や，遺伝子頻度の違いを明らかにした．今回は国内諸地域における集団について，その遺伝子頻度に基づいた地理的勾配の有無を明らかにすることを企て本研究を行った．

国内の7つの地域集団（秋田，宮城，大阪，三重(津)，三重(神島)，長崎，沖縄(石垣)）を対象として，9 Gm システム (Gm a, x, f, b^1, b^3, s, t, g, z) を用い検討した．これらの集団は，東北地方から沖縄にわたる7つの集団であって，血球酵素型のあるもの，たとえば s-GPT 型にみられるような地理的勾配が期待された．しかし，各集団にみられる4つの haplotypes (Gm^{agz}, Gm^{axgz}, Gm^{ab^3stz}, $Gm^{afb^1b^3}$) の頻度に基づいて集団間の等質性の検討を行ったが，地理的勾配は見出されなかった．すなわち，Gm パターンからみると，これらの集団はほぼ等質といえる．

83. **Tasuku TOYOMASU, Kazumichi KATAYAMA, Hideo MATSUMOTO** (Dept. Legal Med., Osaka Med. Sch., Takatsuki) **and Atsushi GOTOH** (Dept. Public Health Jichi Med. Sch., Tochigi): **Human Gen etical Study of Distinctive Populations in Terms of Exposure to HBs Antigen. (II).**

The distribution of red cell enzyme polymorphic traits in three local populations on two islands belonging to Toba City, Mie Pref. were investigated. Estimated allele frequencies so far obtained are:

Kamishima (n, 365) $AcP^{A}=.223$; $PGM_1^1=.748$, $PGM_1^2=.251$, $PGM_1^7=.001$; $EsD^1=.669$; $ADA^2=.011$; $Gpt^1=.533$; $PGD^C=.131$; $Got^2=.001$; $PHI^8=.003$.

Toshi (n, 287) $AcP^{A}=.188$; $PGM_1^1=.771$, $PGM_1^2=.198$, $PGM_1^7=.030$, $PGM_1^6=.002$; $EsD^1=.720$; $ADA^2=.082$; $Gpt^1=.626$; $PGD^C=.146$; $Got^2=.003$, $Got^8=.003$; $PHI^5=.002$.

Momotori (n, 234) $AcP^{A}=.205$; $PGM_1^2=.731$, $PGM_1^2=.252$, $PGM_1^7=.017$; $EsD^1=.748$; $ADA^2=.050$; $Gpt^1=.588$; $PGD^C=.096$; $Got^3=.002$. LDH, Pep. A & B, PGK and AK systems were found to be non-polymorphic in these populations.

As previously reported (Takahisa *et al.*, 1975), the positive rate of exposure to HBs antigen and the presence of antibody in the inhabitants has been demonstrated to have marked regional differences in these area. The authors examined the distribution patterns of each system either in HBs antigen positive groups or anti-HBs antibody positive groups. The patterns show no marked deviation from those expected in each system.

Though the sample size is still not so large, in addition to our previous finding of non-interaction between ABO or Hp *vs.* HBs antigen infection (Toyomasu *et al.*, 1975), there seems to be hardly any correlation between enzyme genetic traits and the susceptibility to antigen infection or immune response. The regional differences in some traits could be explained by the result of a random drift.

〔追加〕 **柳瀬敏幸**(九大・一内): 小集団の生化学的形質の表現型または遺伝子頻度をみる場合に, 一応 sib correlation を消却するよう配慮されるとよいと思う.

84. **安田徳一** (放医研・遺)・**辻　公美** (東海大・医): **HLA と胃がんの関連について.** Norikazu YASUDA (Div. Genet., Nat. Inst. Radiol. Sci., Chiba) and Kimiyoshi TSUJI (Blood and Tissue Typing Center, Tokai Univ., Kanagawa): **An Association between HLA and Gastric Cancer.**

種々の疾患群において, 特定の HLA 抗原が多く (あるいは少なく) 存在するという事実はこの方面の研究に拍車をかけている. とくに生物学的機能により, HLA には, (i)SD 抗原 (A, B, C 座位), (ii)LD抗原 (D座位), (iii)補体 (Bf, C2, C4 座位), (iv)免疫応答遺伝子 (I_r), (v)免疫関連抗原 (I_a) などがあるといわれ, これらが疾病の病因として, それぞれ関連があると思われる. 特に I_r, I_a 遺伝子は HLA と相同なマウスの H2 座位の研究で乳がんやある種の白血病への感受性が

確立されて以来，ヒトでも研究されるようになった．このことは，ヒトで多くの疾患がB座位抗原と関連があることから，I_r または I_a 遺伝子が疾患に関与しているのではないかと疑いをもたせる．今回の報告はこれらの事実にもとづき「HLA-A, B ハプロタイプとB座位近傍の I_r または I_a（あるいはその他）遺伝子が連鎖不平衡にあって，特定の AB ハプロタイプが胃がん患者に多くあらわれる」という仮設を検討した．健康人355名，胃がん患者87名について14種のA抗原，18種のB抗原をmicrocytotoxicity 法で同定した．各座位の抗原頻度，AB ハプロタイプ頻度，連鎖不平衡値は最尤カウント法によった．統計的に有意な抗原は，AW30/AW31, B5, BW16, BW35 がいずれも胃がん患者に少なく，B18 は胃がん患者に多い．連鎖不平衡値の絶対値が 0.01 以上の AB ハプロタイプで両群にあらわれたものは *A2, BW40*, *A9, B5*, *A9, B7*, *A9, B blank*, *All, B5* いずれも胃がん患者に多く，連鎖不平衡値も大きくなっている傾向がみられた．胃がん患者2名のいる一家系では両者とも *A2, BW49* ハプロタイプをもち，集団調査の結果と矛盾することはなかった．

〔追加〕 **笹月健彦**（東京医歯大・難研・遺伝生化）：HLA と疾患との相関のメカニズムとして免疫応答遺伝子を推定するのなら，D座位抗原のタイピングを行って，B—Dハプロタイプと疾患との相関をみるべきと思う．

85. **工藤昭夫**（九大・理）・**林　健児**・**東　晨児**（東京理大）：**家系情報の蓄積と検索のための光学読取カードの設計**．Akio KUDO (Kyushu Univ., Fac. Sci, Fukuoka), Kenji HAYASHI and Shinji AZUMA (Tokyo Science Univ., Tokyo): **Design of Optical Mark Card for Storage and Retrieval of Information Involving Pedigree.**

標記の目的のために光学読取カードを試作し，ひろく人類遺伝学研究者の批判を仰ぐが，このカードは次の利点を持つと考える．（1）鉛筆を用いて系図を描く要領で記入できて，視覚的に眺めることができる．（2）消ゴムを用いての修正が容易であるので，調査の途中での解析ができる．（3）計算機に読み取らせる必要のないもの，または，個人秘の事項を赤鉛筆で記入することができて秘密が守れる．（4）コーデング，およびパンチの手間を省くことができる．（5）記入方法はいくぶん複雑ではあるが，計算機で誤記入のチェックがある程度可能である．

本年度は，親子・同胞関係と遺伝病の有無，出生順位などに重点をおいてカードを設計した．カードの種類は6種類である．

1. 家系カード（表紙に相当する）
2. 系図カード（4代上にさかのぼる系図の図示）
3. 同一個体カード（近親婚があるときに用いる）
4. 同胞カード（同胞を5人並べる）
5. 個人カード，6．流死産個体カード（どちらも各個人についての情報を記入）

1〜3 は各家系に1枚，4〜6 は必要枚数だけ用いる．エラーチェックのプログラムの作成が進行中である．

86. **Itsuro NISHIGAKI, Reiko TSUKAHARA, Kazuo MANO, Norio FUJIKI** (Dept. Epid. Genet., Inst. Develop. Res., Kasugai), **Naofumi OHNO** (Dept. Med., Ehime Univ., Matsuyama), **Howard B. HAMILTON, Chiyoko SATOH, Miyoko MASUMOTO, Akiko TAKETANI, Junko YAMASHITA, Yasukazu KIMURA, Noboru KOSAKA, Takaji NISHIZAWA, Fumiharu SUGINO and Yoshiko NAKAHARA** (Rad. Eff. Res. Found., Hiroshima): **Population Genetic Study in Isolated Communities (III)-Sagishima.**

We have been engaged in population genetic studies in certain isolated communities in Western Japan for over 15 years. This year, we report preliminary data obtained from a field survey in Sagishima (2,000 inhabitants in four villages), Mihara City, Hiroshima Prefecture, although the study has not yet been completed with respect to the identifying and classifying inbreeding structures through Koseki checking.

Among 884 inhabitants in 220 households in Sagi-Sunami area in Sagishima Island, we have conducted medical surveys among 480 inhabitants (approximately 54%) and collected 286 blood samples.

Routine physical and hematological examinations revealed a slightly elevated prevalence of anemia in females and a slight increased frequency of gastrointestinal diseases, the latter possibly ascribable to increased homozygosity of autosomal recessive genes due to consanguineous matings.

The gene frequencies of certain genetic polymorphic traits, are $I^A=0.287$, $I^B=0.233$, $Hp^1=0.335$, $PGM_1^2=0.370$, and $PGD^B=0.061$. Slight differences between these values and those of neighboring populations and other isolated populations suggest an effect of genetic drift and inbreeding operating in a population of small size.

87. **古庄敏行** (鹿大・医・衛生)・**田中克己** (東京医歯大・難研・人類遺伝): **原爆被曝者の子の性比.** Toshiyuki FURUSHO (Dept. Hyg., Kagoshima Univ., Kagoshima) and Katumi TANAKA (Dept. Human Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo): **Sex Ratio in Offspring of Atomic Bomb Survivors.**

1974年，本学会で報告した資料のうち，同胞全員が20歳以上に達した家系から，非被曝群約 2,500家系，被曝群約2,500家系を抽出して，戸籍を用いて同胞全員の性，生年月日，死亡年月日，結婚年月日などを調査している．これらの資料のうち，現在調査完了した分について，非被曝群，父のみ被曝群，母のみ被曝群の3群に分け，子の年齢別に性比および死亡率を計算した．性比は非被曝群で，0.49～0.50，父のみ被曝群で 0.54～0.55，母のみ被曝群で 0.51～0.52 であった．非被曝群と父のみ被曝群の性比は，父のみ被曝群の方が統計的に有意に高いが，非被曝群と母のみ被曝群の間の性比は差がみられなかった．これらの結果，ほぼ遺伝仮説と一致する．

一方，死亡率は例数が少ないので，男女別に1歳未満および20歳未満の2群に分けて比較した．数

字の上では被曝群の方が非被曝群に比べて死亡率は高い．特に20歳未満群の父のみ被曝群での死亡率は女児の方が男児より高い値を示している．しかし，いずれも統計的有意水準には達しない．本研究はまだ調査例数が少ないため，決定的なことはいえない．今後さらに調査例数を増して詳細に検討する予定である．

88. **野原　年・古庄敏行**（鹿大・衛生）・**谷村雅子**（東京医歯大・難研・人類遺伝）：**混血児の研究．I. 身体計測値**．Toshi NOBARA, Toshiyuki FURUSHO (Dept. Hyg., Kagoshima Univ., Kagoshima) and Masako TANIMURA (Dept. Human Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo): **Study on Hybrid Children in Okinawa. I. Measurements.**

昭和48年，沖縄本島の小学校，中学校，高等学校の在学生および卒業生の混血児について学校に保管されている身体検査票から，身長，体重，胸囲，座高の逐年調査測定値を収集し，対照群と比較検討した．一般的に混血児群（白人，黒人，比島人）の方が対照群に比べて大きい値を示した．これらの資料のうち，昭和25～28年に出生した群について，年齢別，性別に対照群と混血児群の平均身長，体重，胸囲，座高を比較すると，男女とも，平均身長，体重，胸囲は対照群に比べ混血児群の方が大きい傾向を示した．しかし，混血の種類によっては一定の傾向を示さなかった．また，座高は，両群間にほとんど差がみられなかった．いずれにしても，なお調査続行中であるから，調査完了時点において改めて詳細に分析し，検討することにし，ここでは中間報告にとどめたい．

89. **Tsutomu MIYASHITA, Koji OHKURA** (Dept. of Human Genet., Tokyo Med. and Dent. Univ., Tokyo), **Hideo MATSUMOTO** (Dept. Forensic Med., Osaka Med. College., Osaka), **Yun Sun KANG and Chung Choo LEE** (Dept. Zool., Seoul National Univ., Seoul): **The Distribution of Polymorphic Traits in Korea.**

Since 1973, we have analyzed several polymorphic traits to compare the genetic structure of Korean populations. So far, 8,892 blood specimens were obtained from eight populations (Kwangha-Do, Seoul, Wonju, Chonju, Taegu, Kyungsan, Kwangju and Pusan) in Korea. In addition, we obtained 831 blood specimens from Cheju which is the Island situated in south of Korean peninsula and having a different history from the peninsula.

Only one case of hypocatalasemia was screened from 831 specimens and the gene frequency of acatalasemia was estimated as 0.0006. Then totaly 9,929 blood specimens were screened (1973-1976) for hypocatalasemia and 21 hypocatalasemics were found. The average gene frequency of acatalasemia in Korean populations is estimated as 0.0011. This value is almost the same as Japanese. The following results of analysis in several blood groups were obtained from 200 specimens in Cheju. ABO: $p=0.232$, $q=0.285$, $r=0.483$. MNSs: $MS=0.0343$, $Ms=0.4822$, $NS=0.0110$, $Ms=0.4665$. Rh: $R^1=0.623$, $R^2=0.298$, $R^0=0.003$, $R^z=0.030$, $r=0.045$, $r'=0.003$. Diego: Di(a+)=10.00%, Duffy: Fy(a+)=98.00%, Fy(b+)=17.50%, Kell:

K+=0%, Kidd: Jk(a+)=43.50%, P: P+=26.00%. The gene frequency of Hp^1 was estimated as 0.299 among 284 specimens and also PGM_1^1 was estimated as 0.759 among 286 specimens.

The clear geographic cline from north to south (Seoul-Chonju-Kwangju-Pusan) was found in ABO (*B* gene), MN (*M* gene) and Rh (R^1 gene) blood groups. But this cline does not continue to Cheju. This result may depend upon the historical difference in the formation of the Cheju and other Korean populations, because it is said that Cheju-Do was conquered in 13th century by Mongol since then the conquerors have settled down in the Island.

90. **Keiichi OMOTO** (Dept. Anthrop., Univ. Tokyo, Tokyo), **Shogo MISAWA, Shoji HARADA** (Inst. Commun. Med., Tsukuba Univ., Ibaraki), **J.S. SUMPAICO, P.M. MEDADO** (BRL, Dep. Health, Manila) **and H. OGONUKI** (JICA, Manila): **Some "Rare" Red Cell Enzyme and Serum Protein Variants Discovered in Polymorphic Frequency among Negritos of Philippines.**

Blood samples of 129 Negritos living in a village near Angeles City, Pampanga, Central Luzon, have been typed for red cell enzyme and serum protein systems by electrophoresis. 9 among 15 red cell enzyme loci scrutinized, while 4 among 5 serum protein loci, showed polymorphisms. Average heterozygosity of the 20 loci examined was calculated to be 0.17. This value is higher than the corresponding value of 0.14 for the Japanese, and it is interesting that such a relatively high degree of variability is found in a small, isolated group such as the Negrito.

Furthermore, it was discovered that three systems, namely, red cell esterase D (ESD), adenylate kinase (AK) and serum group-specific-component (Gc), had "rare" variant alleles, each of which attained polymorphic frequencies. In ESD, a variant allele determining an isozyme, which is migrating much more slowly than ESD-1, had a frequency of 0.10, while ESD^1 and ESD^2 allele frequencies were 0.78 and 0.12, respectively. The variant allele was tentatively called $ESD^{Negrito}$. All the six phenotypes expected were observed and there was no deviation from the Hardy-Weinberg's equilibrium. This seems to be the first example in which three ESD alleles occur in polymorphic frequency. In AK, a variant allele had a frequency of 0.07, what is quite unusual for this system in Asian-Pacific area. Only heterozygote was encountered which is indistinguishable from AK 2-1. In Gc system, a variant component migrating faster than Gc 1 was discovered in all the possible combinations with the two common components, Gc 1 and Gc 2, giving rise to 6 phenotypes in all. The allele frequency for the variant was 0.20, while those for Gc^1 and Gc^2 were 0.63 and 0.17, respectively. The observed numbers were in

agreement with the expected numbers. The variant Gc component was indistinguishable from Gc Aborigine by immunoelectrophoresis, although comparisons by immunofixation are under way.

As hunter-gatherers, the Negritos of Philippines are considered to have inhabited a wide range of area until historical times, scattered in partly isolated breeding units. On the other hand, they must have had considerable amount of gene flow among each other, as their hunting-gathering habits indicate. We consider that these conditions may explain, at least partly, the relatively high degree of genetic variation found in the Negritos.

A more detailed investigation on a larger material recently obtained from various parts of Philippines is in progress in order to elucidate the degree of genetic variablility and, if possible, the genetic origins of the Negritos.

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91. **谷村雅子・田中克己** (東京医歯大・人類遺伝): **近親婚の家族集積**. Masako TANIMURA and Katsumi TANAKA (Dept. Hum. Genet., Tokyo Med. and Dent. Univ., Tokyo): **Accumulation of Consanguineous Marriages within Family.**

夫婦間，夫の両親，および妻の両親における近親婚を調査した日本の4地区の資料を文献から集めて，この3組の夫婦間に近親婚の有無に関し相関があるか否かを分析した．

(1)夫婦・夫の両親・妻の両親の3者間の近親婚に関するnon-random性：3組の夫婦の近親婚の有無により8群に分け，3者間の独立性を仮定した期待値と観察値とを比較したところ，いずれの地区においても有意差があり，特に3組とも近親婚の組合せの観察値は期待値に較べ非常に高かった．

(2)夫婦の両親間の近親婚に関する相関：夫の両親と妻の両親における近親婚の有無により夫婦を2×2群に分け，χ^2 検定を行ない，これら2組の夫婦の近親婚の有無に関し相関を示すか否か調べた．4地区中3地区は有意であり，連関係数が0.322の地区もあった．

(3)親子間の近親婚に関する相関：(2)と同様に4群に分け夫婦の近親婚率を比較すると，最も高いのは(a)夫の両親・妻の両親がともに近親婚の群で，次は(b)片方の両親のみが近親婚の群であり，(c)両方の親が非近親婚群は最も低く，(a)群は(c)群の約3倍であり，この傾向は4地区とも同じであった．また，夫婦間の平均親縁係数は(a)群が(c)群より0.01以上も高かった．

以上より，近親婚の家族内分布はrandomでなく家族内に集積する傾向があると思われる．夫婦間に近親婚がある場合，夫婦の親にも近親婚があると親縁係数が高まることがあるが，夫婦の近親婚と夫または妻の両親の近親婚との間ならびに夫の両親の近親婚と妻の両親の近親婚との間にも相関があるため，親縁係数は著しく増加する．近親婚の相関による親縁係数の増加は2地区において約0.003と推定され，集団平均親縁係数0.01の約30%に相当する．

〔追加〕 **工藤昭夫**(九大・理)：このデータは統計学では2×2×2表として解析できる．このとき，ロジットモデルを用いるのがよいであろう．理由は，ロジットモデルを用いると，相関関係を数値で表現することが可能であるからである．Re-analysisを行えば興味ある結果が出るものと予想する．

92. **Yoko IMAIZUMI** (Inst. Pop. Problems, Ministry of Health and Welfare, Tokyo): **Incidence of Spina Bifida and Parental Consanguinity in Japan.**

An analysis of 1,012 cases of fetal and postnatal deaths with spina bifida during 1969-1974 is presented. Incidence of spina bifida was observed 0.79 per 10,000 total births. The incidence of spina bifida in fetal deaths and postnatal deaths seems to be independent of the maternal age. On the other hand, the incidence of spina bifida in fetal deaths seems to increase linearly with the mother's age. The highest incidence of spina bifida was found in the Kyushu District, whereas the lowest value was found in the Hokkaido District. The incidence of spina bifida in May showed the highest value and lowest in October. The incidence of spina bifida in class I (Agriculture only) of occupation of the head of household showed the highest value, and in class III (Self employed) the lowest one. The rate of first cousin marriages among the parents of patients with spina bifida is 1.29 per cent (3/232).

〔追加〕 **自見庄三郎**(九大・第1内科)：沖縄県における死産率および乳児死亡率は，届出に問題があり，人口動態統計上は，実際より低く出てくる．二分脊椎による，死産および死亡が沖縄県で少ないのはこのためでないか．

93. **蒲生　忍・川辺昌太**（神戸大・理）**・大浦敏明**（大阪小保センター）：**日本におけるフェニールケトン尿症の遺伝子頻度について**. Shinobu GAMOU, Masata KAWABE (Dept. Genet., Kobe Univ., Kobe) and Toshiaki OHURA (Children's Med. Center of Osaka-city, Osaka): **Gene Frequency of Phenylketonuria in Japan.**

文献検索による方法と，アンケートによる方法の2つによって，フェニールケトン尿症（PKU）患者，222名，125家系の資料を集め，遺伝学的解析を行い，遺伝子頻度の推定を試みた．

PKU 患者の性比は，M/F＝106/113，発端者における性比は 62/63 であり，理論値 1/1 によく一致する．分離比の検定には同胞法を用い，常染色体劣性遺伝の理論値25%とよく一致する値23%を得た．また出生順位にもかたよりは認められない．

1965 年に田中らによって行われた PKU の全国的な調査と比較すると，患者両親の近親婚率の低下や，近親婚の形態の多様化が認められる．そこで，従来用いられているいとこ婚のみに注目した Dahlberg の方法に加え，1966年に藤田によって考案された遺伝子頻度の推定式を用い，近年の一般集団における近親婚率の急激な減少をも考慮にいれ，遺伝子頻度の推定を試みた．その結果，0.00767～0.00392 の遺伝子頻度，1/15,000～1/55,000 の患者発生頻度の推定値を得た．推定値は，広い範囲を持っており，どの値がより現実に近いものかは断定できないが，少なくとも，現在マススクリーニングの対象となっている集団では，下限に近い値，すなわち遺伝子頻度0.004，患者発生頻度1/55,000ではないかと考えている．

〔追加〕 **田中克己**（東医歯大・人類遺伝）：私は2回にわたって PKU の遺伝子頻度の推定値を発表したが，今から考えると一般集団の近親婚の減少に気づかなかったため不正確であった．

94. **藤木慶子・田辺歌子・中島　章** (順天堂大・眼)・**安田徳一** (放医研・遺)： **先天性盲における遺伝的荷重.** Keiko FUJIKI, Utako TANABE, Akira NAKAJIMA (Dept. Ophth., Juntendo Univ., Tokyo) and Norikazu YASUDA (Div. Genet., Nat. Inst. Rad. Sci., Chiba): **Genetic Loads on Congenital Blindness.**

近年におけるわが国の近親婚の減少は著しいものがあり，また同時に若年の視覚障害者の頻度もこの10年に急激に減少している．本研究は，この事実と先天性盲の遺伝的荷重との関連を知るために，1954～1970年にわたる5年ごとに行なわれた全国盲学校生徒の失明原因調査資料を用いて，両親のいとこ結婚の頻度から調査年代別に遺伝的荷重の計算を行なった．その結果，任意交配集団が持っている荷重Aは，1954，1959，1964，1970年の資料において，それぞれ 0.00212±0.00002，0.00203±0.00002，0.00207±0.00002，0.00186±0.00002，全荷重 A＋Bは 0.1164±0.0195，0.0751±0.0086，0.0756±0.0084，0.0837±0.0146 であった．これらの値に対する回帰係数は，Aは −0.000014±0.000006，A＋Bでは 0.00080±0.00036 となり，いずれも年代による有意な変化は認められなかった．このことは一般集団中の近親婚の著しい減少にもかかわらず，先天性盲についての劣性遺伝子頻度はほとんど変わらないことを示す．一方，先天性盲における全荷重は 0.15～0.17/zygote と推定され，これは先天性聾，0.04/zygote (Furusho & Yasuda, 1973) の4倍，生後12年までの死亡率から求めた致死相当量 1.3～1.5/zygote (Yamaguchi *et al.*, 1970) の 1/10 に相当する．また B/A の数値の大きいことから，かくれた荷重の大部分が mutation によるものと解釈される．

以上，算出された遺伝的荷重の値，および男女の発病年齢，性差を示す内容の検討については，個々の疾患の遺伝様式の検討とともに今後さらに検討して行きたい．

95. **Takashi TANIMURA** (Dept. Anat., Kyoto Univ., Kyoto) **and Osamu TANAKA** (Hum. Embryo Ctr. Teratol. Stud., Kyoto Univ., Kyoto): **Twin Embryos in Japanese.**

Twins are precious research objects in human genetics and developmental biology but few systematic studies are available on the embryonic stage of twins except one by Corner (1955). Twin conceptuses may be mistaken as singletons if one of the pair is severely damaged in the course of operation for induced abortion in the early stage of pregnancy. Moreover, the fetal membranes are also usually damaged and the diagnosis of zygosity is practically impossible after fixation.

Among the collection of a large number of human embryos and early fetuses in the Human Embryo Center for Teratological Studies, we found 89 pairs of twins in the embryonic stage (Carnegie stages 12 to 23, 4 to 8 weeks of age) and 6 pairs in the early fetal stage (CR length: 30-40 mm). Most of them is fixed in Bouin's fluid and no precise description of the fetal membranes are available. Therefore, in no cases except double monsters zygosity has been established.

The frequency of twin pairs is 0.38% (78/20,417) for the embryos obtained by induced abortions, 1.6% (7/448) for those by spontaneous abortions and 1.8% (4/220) for those by ectopic pregnancies, respectively, while the frequency of twin preg-

nancies at and over the 4th month of pregnancy is reported to be 0.635% according to Vital Statistics 1966-68. The lower frequency of twin embryos in the induced abortion group may be due to loss of severely damaged specimens in one of the twin embryos. A higher prevalence of twins is reported in the ectopy than in the intrauterine pregnancies (*e.g.* Kawashima *et al.*, 1958). The present study also indicates a similar tendency but it may be explained due to more easiness of recognition of both twins in ectopic pregnancies or spontaneous abortion.

Among 78 pairs of twin embryos obtained by induced abortion, both twins are alive in utero in 64 cases (2: polydactyly in one of the pair), one of the pair dead in utero in 2, and both dead in 12 (2: double monster). Among 7 pairs by spontaneous abortion, both are alive in 1, and both dead in 6 (1: double monster, 1: both exencephaly and cleft lip, 1: cleft lip in one of the pair). Among 4 pairs by ectopy, both are alive in 1, one of the pair dead in 1, and both dead in 2 (1: double monster, 1: cleft lip and hydromyelia in one of the pair). As for 6 pairs of early twin fetuses, 3 are externally normal and alive in utero while 3 are dead in utero (1: double monster, 1: oligodactyly in one of the pair).

Comparison of maternal reproductive history of twins (64 cases, both alive in utero, induced abortion) with that in the single embryo group (3084) gave the following results (maternal age, 30.8 ± 5.5 in twins *vs* 31.2 ± 5.7 in singleton; number of previous induced abortions, 1.2 ± 1.4 *vs* 1.2 ± 1.6; number of spontaneous abortions, 0.30 ± 0.74 *vs* 0.20 ± 0.57; number of live births, 1.51 ± 0.90 *vs* 1.74 ± 1.06, $p<0.05$).

Carnegie developmental stage was compared between each pair of twins (induced, both alive in utero). One stage difference roughly corresponds to 2 days in development. No stage difference was noted in 46% of the pairs and one stage difference was observed in 48%, while in 4 cases (6.5%) stage difference by 2 to 4 was recorded.

Comparison of embryonic age between twin embryos (51 cases, induced, alive in utero) and singletons was attempted by checking calculated ovulation age in twin pregnancies *vs* standardized age in singletons equivalent to the mean developmental stage of the twin pair. The development of the twins is retarded in 23 cases (45%) as compared to the singletons, equal in 10 cases (20%) and advanced in 18 cases (35%). This means that the twins are retarded by 1.5 days in average as compared to the singletons. Comparison of body length between twin embryos and singletons showed no appreciable difference if the developmental stage is the same.

96. **Kohei SHIOTA and Ei MATSUNAGA** (Dept. Human Genet., Natl. Inst. Genet., Mishima): **Holoprosencephaly in Human Embryos: An Epidemiologic Study.**

Among the large collection of human embryos in the Human Embryo Center for Teratological Studies of Kyoto University, 150 cases of holoprosencephaly (cyclopia-arhinencephaly series) were found during the period between January 1962 and December 1974. The incidence of the defect in the embryos was 4.1 per 1,000 against 0.06 per 1,000 newborns, which implies that almost all of the affected embryos are destined to be eliminated prenatally. Although no epidemic was noticed, the annual incidence apparently increased slowly from 1963 to 1973.

Possible correlation of the defect with several factors working prior to or during pregnancy was examined by means of the obstetrical record of each specimen. The mean maternal age for the cases was 30.2±5.4 (S.D.), while that for the general population of normal embryos matched with the cases for parity was 29.7± 6.5. When maternal age was matched, the mothers of the cases had significantly lower mean parity than expected (3.6 *vs.* 4.0). However, the mean age of the mothers with lower parities (1 and 2) was significantly higher and the mean number of previous miscarriages for multiparous mothers was significantly greater than expected, suggesting that the "lower" mean parity of the study mothers might be due to unrecognized miscarriages. These results indicate that the mothers having a holoprosencephalic embryo have a tendency of recurrent abortions, for which either genetic and/or chronic maternal conditions may be responsible.

Although the frequency of maternal genital bleeding and of maternal intake of progestogens during the terminated pregnancy showed a higher value among the cases, these factors were regarded as a symptom of having a malformed embryo and its treatment, respectively. No association of holoprosencephaly was verified with paternal age, parental consanguinity, irregular menstrual cycles, maternal diseases, maternal consumption of drugs other than progestogens, and maternal smoking and alcohol consumption.

97. **矢橋弘嗣** (十三市民病院)・**竺原俊行** (今宮市民病院)・**木寺克彦** (北市民病院)・**鶴原常雄** (小児保健センター): **遺伝相談システム—大阪市におけるネットワークについて.** Hirotsugu YAHASHI (Jyuso Municipal Hosp., Osaka), Toshiyuki ZIKUHARA (Imamiya Municipal Hosp., Osaka), Katsuhiko KITERA (Kita Municipal Hosp., Osaka) and Tsuneo TSURUHARA (Child. Hosp., Osaka): **The Network System for Genetic Counseling Servis in Osaka City.**

住民が福祉の充実を望む傾向はますます顕著になってきており，このような住民の中で遺伝相談は

多くの市民の関心を呼んでいる．

大阪市においても，このような市民の要望にこたえて，市民の健康管理，医療にたずさわる保健所26カ所，市民病院5カ所，母子センター，小児センター各1カ所，市立大学医学部を有機的かつ総合的に運営し，遺伝相談を行うためのシステム化，そのネットワーク作りを行っている．これらの施設が遺伝相談の場においてはたすべき役割はそれぞれ異なったものがあり，その特色，役割を十分はたすことにより遺伝相談は充実したものになると考えられる．

このシステムによる遺伝相談の流れは，保健婦が市民の中に入り込んで，その足で堀りおこした．「遺伝に関するものかも知れない」と市民が考えている心配は，先ず保健婦によって窓口相談が行われる．そこから送られた市民病院では，ふるいわけが行われ，センターの専門別相談へと送られる．センターでの専門相談には大学の知識と研究が投入される．

このような遺伝相談の流れ，大阪市における遺伝相談システムをささえるのは保健婦の協力であり，彼女たちがいかに遺伝相談の専門家としての実力を身につけているかが，このシステムの成功のカギを握っているといっても過言でないので，大阪市に勤務する約290人の保健婦全員に遺伝相談の研修を行うべく，カリキュラムを作製し，研修を実施している．

98. **中村キミヱ・川合優子・田村登輝子・池田孝三**（札幌・中央保健所）・**折居忠夫・佐藤重夫**（札幌医大・小児科）・**岡田守夫**（札幌・北保健所）・**荒島真一郎**（北大・小児科）：**保健所での遺伝相談**．Kimie NAKAMURA, Yuko KAWAI, Tokiko TAMURA, Kozo IKEDA (Sapporo Central Health Center, Sapporo), Tadao ORII, Shigeo SATO (Dept. Pediat., Sapporo Medical Collag, Sapporo), Morio OKADA (Sapporo Northern Health Center, Sapporo) and Shinichiro ARASHIMA (Dept. Pediat., Univ. Hokkaido, Sapporo): **Genetic Counseling on the Health Center.**

わが国の小児保健の水準は戦後著しく向上し，近年に至って感染性疾患や栄養障害など外因による疾患が激減し，それに代って遺伝性の原因による疾患や異常が相対的に大きな比重を占めるにいたった．また世論としてサリドマイド奇形児の出現以来，先天異常の問題がクローズアップされ，近年の医学知識の大衆化と家族計画の普及に伴う産児数の急激な減少が先天異常に対する親の関心を高めたと考えられる．そのため，遺伝に関し不安をもつ親たちの要望に応ずるため遺伝の相談業務の必要性が出てきた．札幌市中央保健所および北保健所では全道的に展開されている「不幸な子供を生まない市民運動」の一環として，昭和48年1月より予約制で遺伝相談を行っている．昭和51年10月現在，中央保建所で141例，北保健所で52例の件数があり，相談内容は近親婚の可否，精神病，精薄，奇形，妊娠中の胎児に関するもの，羊水診断などであった．また来訪者のうち，約半数が本人で，36%が母親であった．年齢的には20歳代女性が60%をしめ，ついで30代女性と20～30代女性が圧倒的に多かった．遺伝性でない病気を遺伝する病気と考えたり，来訪者のいう病名と医師の診断名が異なるなど誤った考えから，また未知から生まれてくる不幸な子供たちの出生を少しでも多く防止するためにますます遺伝相談の重要性を認識しているが，さらに保健所での遺伝相談の問題点について報告した．

〔追加〕 **多田啓也**（大阪市大・小児）：遺伝相談をやって痛感することは，基本となる疾患の診断の正確さで，例えばハーラー症候群とハンター症候群は臨床症状が酷似しているが，遺伝形式は前者が常染色体劣性，後者が伴性劣性で異なる．クライアントの訴えがハーラー症候群ということであったが，実際患者を調べてみるとハンターであった例を経験しており，カウンセラーと専門医との密接な

協力が遺伝相談にはきわめて重要であることを指摘したい．

〔追加〕 **藤木典生**（愛知コロニー研）：遺伝病の異質性について相談医は慎重に検査し，主治医との緊密な連携による正確な診断が先ず必要であることを，Tay-Sachs 病の私どもの経験からも指摘したい．

99. **松井一郎・黒木良和・須川　豊**（神奈川こども医療センター）：**母子保健展開と遺伝相談**．Ichiro MATSUI, Yoshikazu KUROKI and Yutaka SUGAWA (Kanagawa Children's Medical Center, Yokohama): **Maternal and Child Health System and Genetics Counseling.**

神奈川県逗子市における母子保健ケアーシステムおよび遺伝相談サブシステムを概説した．

現在行なわれている母子保健施策の展開は密度は高いが，心身障害児対策の面で大きな弱点がある．健診は断片的で，集められた情報も追跡的な活用がなされていない．障害児ケアもきわめて不充分である．

逗子市（人口 50,000，年間出生 1,000）で，先天異常の早期発見と治療および療育の一貫した実効的システムに取り組んできた．1）心身障害を中心とすること．2）妊娠時点からハイリスク群を追跡健康管理する．3）医療と療育の効果的提供とその評価．4）濃密な疾病情報の管理，がその骨子である．市役所（保健婦）を中心に保健所，医師会，児童相談所，福祉事務所などとプロジェクトチームを組み実践してきた．

遺伝相談はこども医療センターの1つのサテライトとして位置づけて活動した．過去2年間の経験として，遺伝相談の地域システムを効果的に運用するためには下記の条件が重要であった．1）先天異常診断能力の高い医療機関と連携すること，2）充実した母子健康管理地域システムを育成すること（現在の保健所に遺伝相談窓口を置くだけでは実効性に乏しい），3）遺伝相談でも追跡管理をしないと自己満足に終る可能性がつよく，評価システムを持つことはきわめて重要である．疾病情報管理についても同様，4）福祉ケアの充実で家族にメリットのある具体策を推進させること．

以上のシステムは先天異常モニタリングの機能をも併せもつことになる．

100. **玉木健雄・堀口　隆**（兵・二・病）：**こども病院のケア・システム**．Tateo TAMAKI, Takashi HORIGUCHI (Hyogo Prefectural Kobe Children's Hospital, Kobe): **Care System in Children's Hospital.**

母子保健を，具体的に医療の中に展開するには，現行の医療システム（社会通念も含めて）そのものが，原始医療体系をとっている以上，困難な問題が山積している．

指導相談部は，小児医療の中での母子保健に対処する組織としてユニークな存在であろう．その構成は，医師3名，保健婦2名，ケースワーカー1名，心理判定員2名，栄養士1名，用務事務員3名からなり，業務内容では，生育発達障害に関するもの，母子保健に関するもの，小児精神衛生相談に関するもの，研修講座（衛生教育，専門講座）に関するもの，巡回診療に関するものである．今回述べた巡回診療は，昭和45年開院以来，先天異常を中心とした指導と相談を行ってきている．すなわち，県下特定地域の医療機関と保健所を中心に，第1次検診で問題児が整理され，協議の上で，これに対応して巡回チームが編成され，3者の立ち会いのもとで検診・指導・相談（第2次～第3次検診）が行われ，検診後は，診断・予後・治療について検討会（評価）を実施しつつ，次のステップ（こども

病院受診)を踏み，同時に遠隔追跡調査も行ってきている．45年以来の検診人員は，延べ2120人で，そのうち乳児20.8%，幼児前半60.1%を占め，事後処置については，こども病院への受診は20%に及んでいる．巡回診療の行われる地域には，衛生教育も行いつつ，それぞれの地域の実体も含めて feed back させている．その他の関係機関や行政的な啓蒙啓発と併行して，その成果は49年度以降に見られる母子保健統計上の死産率，周産期死亡，新生児死亡，乳児死亡等の低下に現われ，さらに，モニタリングシステムへの発展が望まれる．

101. **半田順俊**（和歌山医大・解剖）・**大倉興司**（東医歯大・人類遺伝）：**遺伝相談システムの日米における相違と問題点**．Yoshitoshi HANDA (Dept. Anat., Wakayama Med. College, Wakayama) and Koji OHKURA (Dept. Human Genet., Tokyo Med. Dent. Univ., Tokyo): **Genetic Counseling in America and Japan.**

医学教育に人類遺伝学が導入され，遺伝相談にすでに30年の歴史のある米国では，相談部門のある施設は400～450あるという．したがって医師のカウンセラーも多く，現在はその負担を軽減すべく，マスターコースの Genetic associate の養成が行われ，施設に配置されつつある．そして遺伝相談のあり方は，National Genetic Foundation (N.G.F.) の援助によるワークショップの報告 (1974) のごとく，専門家によって位置づけられている．ただ施設ならびにカウンセラーのレベルにはかなりの差があるようであり，一方，カナダでは medical genetist の資格検定を1977年から実施すべく準備が進められている．

遺伝相談ネットワークならびに地域サービスとしては，第1は N.G.F. のネットワークシステムが，カナダを含む54機関によって編成され，ニューヨークの事務所で，クライアントを受入れ，それぞれの機関に紹介するものである．現在はニューヨーク近傍の活動が主で，全国的とはいい難い．第2は Ricardi ら (1975) の報告の地域遺伝相談プログラムで，広汎なコロラド・ワイオミング地区において，あらかじめ genetic nurse により相談資料を整備し，巡回時のカウンセリングを円滑に進める方法で，第3は Epistein ら (1975) の報告の Center Sateliite System で，カリフォルニヤ州全地区に12の satellite clinic を設け，サンフランシスコにある大学の小児科のセンターと連携をとるもので，それぞれの効果をあげている．ただし，行政的な財政基礎のもとの運営ではない．

日本では医学教育に人類遺伝学が本格的に導入されていないので，医師のこの方面の知識が乏しく，カウンセラーの研修は本学会の遺伝相談ネットワーク委員会によって実施されたもののみである．そして，これらのカウンセラーにより，遺伝相談部門が開設された施設がようやく17に達することができた．1977年より，厚生省が遺伝相談を特別家族計画事業としてとりあげる予定となっているので，今後は急速に発展するものと思われる．

102. **大倉興司**（東京医歯大・難研・人類遺伝）：**遺伝的危険率の評価に関する研究**．Koji OHKURA (Dept. Human Genet. Tokyo Med. and Dent. Univ., Tokyo): **Study on Opinion in Evaluating the Genetic Risk.**

一般に日本人は遺伝的危険率の評価が厳しいことは，1975年度の本学会で各種の階層についての調査結果で示したとおりである．遺伝相談において，カウンセラーはしばしばクライアントの不安，心理的かっとう，抑圧を除くのに困難を感じる．それは，注意深く，また合理的な相談を行い，遺伝的危険率について十分に理解のゆくような説明を加えても，なかなかクライアントが心を開こうとしな

いところにある．遺伝的危険率を理解するに当って，十分な時間をとって説明，教育することによって，過度に危険感をもつ者が，いささかでも評価を緩やかにするかどうかは，遺伝相談の結果の成否と関連する．

実際にクライアントについて，遺伝相談の前後で危険率に対する評価の変化を調べることは，個々の遺伝相談においては不可能なので，遺伝相談研修に参加した医師58名，助産婦学校の学生30名，保健婦学校の学生47名について，それぞれ80時間，15時間，6時間の教育の前後での評価を調査した．すなわち，危険率50%，25%，10%，5%，3%，2%，1%，0.5%に対して，それぞれ，非常に高い，高い，中等度，低い，非常に低い，という5段階で評価を行わせた．この結果，保健婦学生ではほとんど評価の変化はなかったが，助産婦学生でやや変化がみられ，医師では相当大きな変化がみられ，評価，特に危険率10%以下に対して緩やかな評価が行われた．危険率の評価，意識を変えさせるには，非常に長い時間を要し，十分な説明を行う必要のあることが明らかになった．

103. **藤木典生・大石英恒・鳥井文恵**（春日井，発達障害研・遺伝）・**小林晴彦**（名古屋・日赤・精神）・**鈴森　薫**（名市大・産婦人科）・**木村　勇**（愛知淑徳大）・**首藤友彦**（名古屋市衛生局）：**遺伝相談（V）**．Norio FUJITA, Hidetune OISHI, Fumie TORII (Dept. Gene., Inst. Develop. Res., Aichi Prefectural Colony, Kasugai), Haruhiko KOBAYASHI (Dept. Psy., Red Cross Hosp., Nagoya), Kaoru SUZUMORI (Dept. Gynecol., Nagoya City Univ., Nagoya), Isamu KIMURA (Aichi Shukutoku Col., Aichi), Tomohiko SUDOH (Dept. Public Health, Nagoya City, Nagoya): **Genetic Counseling V.**

これまでに，京府医大，大阪育児相談室，発達障害研と新たに始めた名古屋市衛生局での遺伝相談例を加えて，1,355 例を数えている．

名古屋市の相談例では，家族の中に遺伝病や奇形があって，その遺伝予後を尋ねてくる40歳以上の女性の多いことが特色で，地域社会の保健の問題について，保健所での相談業務の第一歩として，遺伝相談業務が行われている．そして，ここで遺伝について理解し，不必要な怖れを解消していることが多い．

最後に，相談例について追跡調査を行ってきたが，技術的な問題とともに，相談者自身とその人をとりまく社会の心理的，倫理的問題についても討議する必要性を痛感した．

104. **山形佳伸・松田　博**（愛媛大・小児科）：**「ダウン症児」をもつ親への Information について**．Yoshinobu YAMAGATA and Hiroshi MATSUDA (Dept. Pediat., Ehime Univ., Matsuyama): **On Informing the Parents of Diagnosis of Down's Syndrome.**

「ダウン症候群」という診断をいつ，どのように親へ話すことが望ましいかということは，きわめて難しい問題である．われわれは，実際にわが子がダウン症候群患児（以下「ダウン症児」と略す）であると告げられた人たちの体験から，この問題に対するなんらかの示唆が得られないかと考えアンケート調査を行ない，回答の得られた「ダウン症児」の父59名，母76名について検討を行ない，以下のごとき結果を得た．

結果：生後1カ月から4カ月の間に診断を告げられた者が父 29.6%，母 32.4% で最も多く，生後4カ月から8カ月の間に知った者がこれにつぎ，この2群が約半数を占めたが，生後1カ月までに診

断を教えられたのは父 16.7%，母 9.5% にすぎなかった．この診断を告げられた時期に対し「適当であった」と答えた父は 66.7% であったが，母は 48.0% にすぎず，「不適当」と答えた者のうち，「早すぎた」と答えた第一子が「ダウン症児」であった母4名を除いてはすべてが「遅すぎた」と答えた．そして父の 83.0%，母の 68.0% が生後1カ月までに診断を告げるべきであると考えており，そのとき医師は両親へ同時に話すのが良いと答え，彼らの実際の体験とは大きな差異のあることが分った．

この種の問題に対する明確な結論は得らるべくもないが，われわれはこれらの結果を勘案して，できるだけ生後1カ月までに診断を両親に告げ，その病像の適切な説明をなすべきではないかと考える．

〔追加〕 **塩野 寛**(国立西札幌病院・小児科)：私たちのところでも，北海道のダウン症の両親 122 名にアンケートの回答をもらった．その中で子供を生んだ時点で何か悪い予感がしたかの質問に対して，約 80% の母親は自分の子供の異常に気がついていた．母親の産じょく期のすんだとき，両親一緒にできるだけ早く話した方が良いと思われる．

105. **松本秀雄**（大阪医大・法医）：**興味ある親子鑑定例.** Hideo MATSUMOTO (Dept. Legal Med., Osaka Med. School, Takatsuki): **A Report of the Paternity Case.**

与えられた母子の組合せについて，疑問の男性が父であるか否かを決める父子鑑定において，父たるべき男性が死亡している場合も少なくない．人類学的検査と限られた数の単純遺伝形質によった時代には，その判断にはより多くの困難が伴った．しかし，血液成分について識別される遺伝形質が飛躍的に増加した現在では，父子鑑定は一層の確からしさをもって判断できるようになったといえる．

本例は，父親として訴えられた男が死亡したのちに，いわば第4号夫人にあたる女性がその3人の子供について認知を請求した事件である．本例では，原告である3人の子供とその母，本妻（死亡）との間の3人の子供，第2号夫人とその子1名および第3号夫人とその子2名，計 12 名について，23種類の単純遺伝形質（ABo, MNSs, P, Se, Rh, Kell, Kidd, Duffy, Diego 血球型，HL-A 白血球型，Hp, Tf, Gm, Gc, Km 血清型，AcP, PGM, PGD, ADA, EsD, s-GOT, s-GPT 血球酵素型および耳垢型）の検査と人類学的検査を行った．

本妻との間の3人の実子，2号夫人とその子，3号夫人と2人の子供について，得られた成績から限定された血液型に基づいて，原告3名との間の父子関係の存否を検討した結果，第1子はGm型，s-GOT 型および HL-A 型で，第2子は ABO 式，Gm 型，s-GOT 型および HL-A 型について父子関係が否定され，第3子のみ 99.9% という高い確率で父子関係が肯定された．

106. **本多達雄・大野 剛・高内則夫・竹内正七**（新大・産婦）：**産婦人科と遺伝相談.** Tatsuo HONDA, Takeshi OHNO, Norio TAKAUCHI and Syoshichi TAKEUCHI (Dept. Obst. Gynec., Niigata Univ., Niigata): **The Role of Gynecologist and Obstetrician in Genetic Counseling.**

理想的な遺伝相談システムへの要望がようやく声を大にしてさけばれ始めたとはいえ，現実の状態ではまだまだ私たち産婦人科医が遺伝相談的内容の相談担当者的立場に立たされざるをえない場合が多く，これに対応するためにはその実態を良く知らねばならないとの考えから，(1)一般各層女性が先天異常や遺伝相談に示す関心度，意識の程度・傾向，哲学，道徳観などについて知ること，(2)実

際に産婦人科医を対象として遺伝相談的内容の相談に来訪したものについてその内容を検討し，その特徴を知ること，の2点に目的をおいて調査した．

方法：1) 当科遺伝外来開設（昭和48年2月）以来約3年間にカルテ作成にまで至った180例についてその内容を分析，検討した．2) 新潟市内一般各層女性にアンケート調査を行い，回収した1,341通（回収率79.3%）についてこれを集計，調査した．

結果：1) 産婦人科医による遺伝相談では，その内容の大多数（88%）が妊娠，分娩に直接に関連していた．また，同様にアンケートによる調査でも，一般婦人の約89%が相談相手として産婦人科医を選んでいるとの結果であった．2) 未婚を含め，30歳までの若い婦人のグループでは，それ以上の年齢のものにくらべて，何かにつけ「まず相談してから決める」傾向の強いことを知った．

結論：上記により得られた2つの結果は，現状での遺伝相談における産婦人科医のあり方を示すとともに，将来この方面への need がさらに高くなることを暗示するものと受取れる．

107. **Katsuya TSUDA, Tsutomu YAMANAKA** (Cent. Hosp., Aichi Pref. Colony, Kasugai), **Kaoru SUZUMORI** (Dept. Obst. Gynec., Nagoya City Univ., Nagoya) **and Hidetsune OISHI** (Dept. Genet., Inst. Develop. Res., Kasugai): **Follow-up Study of the Children Undergone Amniocentesis.**

Amniocentesis was carried out in 161 pregnancies from August, 1971 to September, 1976. There were 13 interruptions of pregnancy due to diagnosis of chromosomal abnormalities. The ages of 102 children examined after birth are as follows:

Age	Number of children
Less than 1 year	27
1 to 3 years	48
4 to 5 years	27

The eldest child was 4 years 7 months of age.

Followings are results of examination:

1) Three spontaneous abortions (2%) and 4 premature birth (3.9%) occurred after amniocentesis.

2) In one out of 145 pregnancies, vaginal bleeding occurred after amniocentesis, but no other complications were noted. There were no unexpected complications during pregnancy and delivery after amniocentesis.

3) The incidence of low birth weight infant, small-for-dates infant and excessivily large baby was 5.8%, 3.9% and 3.9%, respectively. These incidences are equal to those of general population.

4) The values of physical measurements in full-term newborn infants were not different from general population. The frequency of minor malformations was not appreciably increased.

5) No harmfull effects were observed on growth and development in subsequent

years up to age 3. The mean of developmental quotient for the group was not significantly different from the normal standardization data for the test. Thirty-one subjects aged less than 1 year had a mean value of 104.7± standard deviation of 12.7 (range 66.1 to 134.0), 50 subjects of age 1 to 3 years 104.0±12.1 (range 70.0 to 131.0) and 19 subjects of age more than 3 years 110.1±15.0 (range 83.3 to 141.0). In 3 instances, developmental score was lower than 75 (2.9%).

6) Congenital abnormalities which were not detectable by amniocentesis were as follows: a case of cerebral palsy, congenital heart disease and congenital subluxation of the hip. Futher studies are necessary to elucidate relationship between these congenital abnormalities and amniocentesis.

7) Questionable needle mark was observed in two cases. One child had a 2 mm dimple in the left upper arm and another in the right leg. But there was no neurological abnormality.

〔**質問**〕 **田村昭蔵**(慶大・産婦)：報告例の中に経胎盤的穿刺を行ったもの，頻回穿刺例は何%くらいになり，それらの例の follow up 成績は如何.

〔**答**〕 **鈴森 薫**：1) 胎盤の前壁付着の頻度について：B-Scan により前壁付着と診断した症例は穿刺例のほぼ 10～20% 位に認められている.

2) 羊水穿刺を再度必要とした症例数について：穿刺前に超音波診断装置 (B-Scan) を併用していない時期には，10% 前後の再度羊水穿刺例が存在した．これらのほとんどは，いわゆる Dry Tap であった．B-Scan の併用後では，2～3% に減少している．この際の穿刺不能例はさきほど述べた前壁胎盤付着が主たる原因で，このような症例に関しては 2～3 週後再穿刺を行っている.

3) 超音波診断装置の利用前後の比較について：この点に関しての児の予後とか種々の問題に関する検討は現段階では充分に行っていないが，以後施行することを考慮している.

〔**質問**〕 **塩野 寛**(国立西札幌病院)：羊水穿刺によって診断された性染色体異常のその後のとりあつかいについてはどう考えるか.

〔**答**〕 **津田克也**：ターナー症候群，クラインフェルター症候群が出生前に診断された経験は今までにないが，ターナー症候群は精神発達正常のことが多く，クラインフェルター症候群も軽度の知能障害が多く，これらの胎児をどうするかについてはむずかしい問題と考える.

108. **斉藤仲道** (九大・産婦科)・**久永幸生**・**正本宗子**・**松尾寿子**・**斉藤ヒサ子** (九大・医療短大)・**名和頭子** (九大・小児科)：**羊水穿刺と児の長期予後に関する検討.** Nakamichi SAITO (Dept. Obst. Gynec., Kyushu Univ., Fukuoka), Sachio HISANAGA, Muneko MASAMOTO, Toshiko MATSUO, Hisako SAITO (Dept. Health Sci., Kyushu Univ., Fukuoka) and Akiko NAWA (Dept. Pediat., Kyushu Univ., Fukuoka): **Amniocentesis and Assessment of Its Long Term Effect upon the Offspring.**

われわれは，1971年以降羊水細胞培養による染色体分析の目的で羊水穿刺を行った131例のうち対象90例に対して母親の意識調査，分娩時の異常頻度，児の身体発育，精神運動発達についてアンケート調査を行ったので，その成績について報告する．意識調査では，出生前診断に対する一般の関心は

低く，その内容について充分理解をえていないこと，また異常であれば中絶を前提としたものと想像される羊水診断に対し，一部にたとえ異常であっても中絶という手段はとりたくないという ambivalent な複雑な感情があることを知った．また 60% 以上が出生前に性別を知らなくともよいと答えていることは，母親が知りたいのは児の異常の有無であることを印象づけている．羊水穿刺群の分娩様式や産科的合併症は一般頻度に比して高率であるという結果はえられなかった．ついで，長期予後としてみた児の身体発育や精神運動発達にも異常を認めることはできなかった．しかし，今回の精神運動発達面の予後調査については2つの限界があった．1つは母親からのアンケート調査であるところから，一部の面接例を除くと専門的，客観的評価が充分であるとはいえないことであり，次に一横断面で異常が疑われた例でも経時的，縦断的に発達を追跡することにより正常であることを確認しえたことから，小児の精神運動発達の一断面のみで予後を評価することには危険があると考えられた．今後は，出生直後より長期にわたって縦断的に発達を追い，非穿刺群との比較検討を行う必要があることが示唆される．

〔**追加・質問**〕 **松本雅彦**（大阪市大・産婦人科）：私どもも小児科多田教室と共同で羊水診断を行っており，実用段階に入った最近3年間で，染色体分析，酵素分析合わせて約180例，それ以前の試行段階のものをもあわせると約250例の羊水穿刺を行った．これらについて現在追跡調査を行っているが，演者と同様に慎重に行われた羊水穿刺は安全と考えている．しかし，遺伝相談のなかで羊水診断を運用してゆくにあたっては，その risk は一般論としてではなく，危険であることを前提として，個々の例において慎重な態度でのぞむことが必要と思われる．

羊水穿刺の risk を話した後，羊水診断を行わなかった例は何%位あったか．

〔**答**〕 **斉藤仲道**：われわれの施設では，90% 以上が小児科および産婦人科医よりの紹介であるため，あらかじめ説明を受けており，決心をしてきている．また，遠路よりの受診者が多いため，特に適応ではないケースは別として，全例検査を行っている．ただし，超音波検査の結果，経胎盤穿刺を必要とするものは，あらかじめリスクについて説明している．この場合，穿刺を断念するものもごく少数例ではあるがあった．