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Abstracts of Papers Communicated at the 26th Annual Meeting of the Japan Society of Human Genetics, 1981

一般講演 General Contribution

A1. Analysis of Lymphocyte Proteins of Patients with Systemic Lupus Erythematosus:

Fumitaka MORITO, Akihide OHTA, Yoichi SETOGUCHI, Toshiro NAGAYOSHI and Masaya YAMAGUCHI (Dept. Intern. Med., Saga Med. Sch., Saga)

The development of systemic lupus erythematosus (SLE) is concerned with genetic and environmental factors. Its hereditary manner is more likely to be compatible with a multifactorial inheritance than a simple Mendelian inheritance.

The mutant genes which have submajor effects on the development of SLE, may produce some special gene products. For the purpose of demonstrating the presence of these particular products, we analyzed the protein components of lymphocytes and fibroblasts from SLE patients and compared with those of normal controls. The total proteins were highly resolved by two-dimensional gel electrophoresis according to the method of O'Farrell and analyzed by autoradiography or silver stain.

When the electrophoretic patterns were compared side by side between normal controls and SLE patients, two polypeptide spots and one polypeptide spot were seemed to differ in their lymphocyte and skin fibroblast proteins, respectively.

The variant polypeptide spot of m.w. 66,000/pI 5.0 in the lymphocyte proteins was decreased and the spot of m.w. 68,000/pI 5.15 in the fibroblast proteins might be disappeared in the patients with SLE. The variant polypeptide spot with m.w. 57,000/pI 5.8 in the lymphocyte proteins seemed to differ in the electrophoretic mobilities between normal controls and SLE patients. It is possible that these variant polypeptide spots might be one of several factors contributed to development of SLE.

A2. Genetic Structure of HLA-D Region: Kiyomi OGAWA, Toshio SONE and Take-

hiko SASAZUKI (Dep. Hum. Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

HLA-D region is assumed to be comparable to I region of the murine H-2 complex, where the genes controlling the immune responsiveness or the disease susceptibility are located. We showed the strong mixed lymphocyte reaction (MLR) between Dw2 and

Dw12, both of which were typed as DR2 serologically, and proposed that HLA-D region was composed of several subregions including HLA-DR locus.

¹⁴C-Labeled membrane proteins from HLA-D homozygous B lymphoblastoid cells transformed with EB-virus were solubilized with detergent and were analyzed with two dimensional gel electrophoresis by using monoclonal antibody to HLA-D region product.

Actin (M.W.=44 K) and Ii molecule (M.W.=31 K) were used as an index in two dimensional gel electrophoresis. Immunoprecipitates from Dw2 and Dw12 consisted of two polypeptides, α (M.W.=32-34 K) and β (M.W.=28-30 K). α -Chains from Dw2 and Dw12 showed the same mobility but β -chains from Dw2 and Dw12 showed different isoelectric point in two dimensional gel electrophoresis. This result indicates that β -chains obtained by the monoclonal antibody to HLA-D region product from Dw2 and Dw12 were different molecules, and this difference may be responsible for the strong MLR between HLA-Dw2 and Dw12.

A3. Genetic Analysis of Human Leukocyte Proteins by Two-Dimensional Gel Electrophoresis. 1. Genetic Variant Polypeptides in PHA-Stimulated Peripheral Blood Lymphocytes: Hideo HAMAGUCHI, Michiko YAMADA, Ryozauro MUKAI, Toshio YABE and Ikuko KONDO (Div. Hum. Genet., Univ. Tsukuba, Ibaraki)

Approximately 250 phytohemagglutinin (PHA)-stimulated peripheral blood lymphocyte polypeptides from three unrelated healthy males were compared by high-resolution two-dimensional gel electrophoresis and double-label autoradiography. Comparisons by all possible pairwise combinations of [¹⁴C]leucine-labeled proteins from an individual and [³H]leucine-labeled proteins from another revealed that only three polypeptides differed qualitatively among the three individuals. Among the three variant polypeptides, the polypeptide with mol. wt. 64,000 coexisted with a polypeptide with the same molecular weight, and they showed the behavior expected of two allelic gene products separated in the isoelectric focusing dimension by charge differences. The polypeptide with mol. wt. 64,000 is a leukocyte cytosol major polypeptide (LC64KPP) and three different commonly occurring electrophoretic types (1-1, 2-1 and 2-2) of LC64KPP have been identified in the population survey. Family studies indicate that they are determined by two alleles at an autosomal locus (LC64KPP). The gene frequencies of *LC64KPP*¹ and *LC64KPP*² in unrelated Japanese adults were tentatively estimated to be 0.93 and 0.07, respectively.

- A4. Genetic Analysis of Human Leukocyte Proteins by Two-Dimensional Gel Electrophoresis. 2. Cell and Tissue Distribution of Polymorphic Leukocyte Cytosol 64 K Polypeptide: Michiko YAMADA, Ikuko KONDO, Keiji FUJII*, Atsuo NOGUCHI**, Toshio YABE, Ryozauro MUKAI and Hideo HAMAGUCHI (Div. Hum. Genet., *Div. Pathol., **Div. Immunol., Univ. Tsukuba, Ibaraki)**

In the previous paper, we reported that human leukocyte cytosol major polypeptide with mol. wt. 64,000 (LC64KPP) shows genetic polymorphisms. In order to obtain the basic data on the physiological role of LC64KPP, the cell and tissue distribution of LC64KPP was examined by O'Farrell's two-dimensional electrophoresis. LC64KPP was prominent in peripheral blood lymphocytes, B-lymphoblastoid cells, T-lymphoblastoid cells, lymph node and spleen. It was also observed in lesser amounts in granulocytes. Only vestigial amount of LC64KPP was, however, found in liver, kidney, cerebrum and skeletal muscle. In addition, no LC64KPP was detected in serum proteins, erythrocyte lysate proteins, [¹⁴C]-leucine-labeled HeLa cell proteins, and [¹⁴C]leucine-labeled diploid fibroblast proteins. The data suggest that LC64KPP is associated with the function and/or the structure of leukocytes and that it is a new polypeptide which shows genetic polymorphism.

- A5. Isolation and Characterization of Amyloid Fibril Proteins from a Case of Familial Amyloidosis: Tomotaka SHINODA, Yoko YAGUCHI (Dept. Chem., Tokyo Metropolitan Univ., Tokyo) Shozo KITO and Eiko ITOGA (Dept. Med., Hiroshima Univ., Hiroshima)**

Amyloid fibril proteins were extracted from amyloid-laden kidney with water, after exhaustive washings of the tissue homogenates with physiological saline containing 0.05% sodium azide, pH 7.0. The water extracts were first lyophilized and degraded with 0.1 M NaOH at 37°C for 20 hr, and the soluble fraction (DAM) was used as samples for further purification: 1) gel filtration on a column of Sephadex G-75 (superfine) using 0.1 M NaOH, 2) gel filtration on a column of Sephadex G-100 in 5 M guanidine-HCl in 1 M acetic acid using fractionated DAMs, 3) ion exchange column chromatography with DEAE-Sephadex A-50 in 0.01 M phosphate buffer-8 M urea, pH 8.6. Finally the fibril proteins were concentrated by lyophilization following the exhaustive dialysis of the samples from ion exchange chromatography against H₂O. The resulting fibril proteins did not react with any antisera against human serum proteins including prealbumin. It existed in three different molecular species with approximate molecular weights of 8,000, 14,000 and over 50,000. The 8,000 component showed isoelectric point of pH 4.2, whereas the other two represented rather broad ranges of pH 4.5-5.8. On electron microscopic examination, they had typical fibrillar forms with different sizes, but their shapes were essentially the same as those present in the original amyloid-laden kidney. Amino acid analysis revealed that these

different molecular species had similar compositions: they are poor in cystine and methionine but are rich in aspartic and glutamic acid, glycine and alanine, respectively. The present data indicated that there are some basic differences between Ogawa Village type hereditary amyloidosis and that in Portugal with regard to their protein species.

A6. Delivery of Fungal β -Galactosidase to Rat Brain by Means of Liposomes: Goro TAKADA, Hitoshi ONODERA and Keiya TADA (Dept. Pediat., Tohoku Univ. Sch. Med., Sendai)

A significant increase in β -galactosidase activity was observed in the brain of rats 1 hr after an intravenous injection of liposomes containing β -galactosidase purified from *Aspergillus oryzae*. The increased activity was proved to have features of the fungal enzyme by differentiating it from rat's native β -galactosidase in both heat stability and immunochemical studies. Blood content of rat brain tissue under our experimental conditions was estimated as 0.82% (v/w) from an infusion experiment of ^{125}I -labeled human serum albumin. The net uptake of fungal β -galactosidase by rat brain was calculated as equal to 10 μg protein of the fungal enzyme or 0.31% of the injected dose/g tissue, which gave rise to 4.4-fold net increase in enzyme activity above control levels. Our experiments clearly demonstrated that liposome-entrapped fungal enzyme was allowed to penetrate the blood-brain barrier and to gain access to rat brain, suggesting liposomes as an effective carrier for exogenous enzymes delivering to the central nervous system of patients with inherited lysosomal storage diseases.

A7. Late Onset *N*-Acetylgalactosamine-6-Sulfate Sulfatase Deficiency in Two Brothers: Tadao ORII, Kazuko SUKEGAWA and Toshiaki TAGA (Dept. Pediat., Gifu Univ. Sch. Med., Gifu)

Two brother patients, aged 25 and 29, both with normal intelligence and absence of central nervous system abnormalities exhibited dysostosis multiplex, cloudy corneas, excessive excretion of keratan sulfate. Their parents were first cousins. They were first studied at ages of 9 and 10 years because of both swinging gait and hip pain respectively.

Radiologically their bony changes can be classified as a type of spondyloepiphyseal dysplasia but they differ from patients with typical Morquio syndrome.

Lymphocytes and fibroblasts of both patients were deficient in *N*-acetylgalactosamine-6-sulfate sulfatase, the deficient enzyme in Morquio syndrome.

Like this, it is indicated that our two brother cases have later onset of clinical abnormalities, milder skeletal deformities and slower progression of the disease.

Therefore, we propose the existence of late onset form of *N*-acetylgalactosamine-6-sulfate sulfatase deficiency.

A8. Enzymatic Abnormality of Alpha-Mannosidase in I-Cell Disease and Mannosidosis:**Takahiro TAHARA and Yoshikatsu ETO** (Dept. Ped., Jikei Univ., Tokyo)

I-cell disease is an autosomal recessive disorder characterized by a defect of lysosomal enzyme packaging into lysosomes. A defect is most recently suggested as a deficiency of UDP-*N*-acetyl glucosaminyl phosphate transferase.

Mannosidosis is also an autosomal recessive disorder characterized by a defect of alpha-mannosidase (A and B).

The present report demonstrates that neutral alpha-mannosidase (C) was deficient or reduced in various tissues, serum and cultured skin fibroblasts from patients with I-cell disease. These are also confirmed by DEAE-Sepharose column chromatography. These data indicate that neutral alpha-mannosidase activity in I-cell disease is involved by a defect of phosphorylation and altered the stability of the enzyme or failed to proceed to the normal processing of alpha-mannosidase.

A9. Prenatal Diagnosis of Tay-Sachs Disease in Cell Free Amniotic Fluid: Momoko**Saito, Shintaro TSUKASA, Osamu NISHIYA, Takeshi SAKIYAMA and Teruo KITAGAWA** (Dept. Pediat., Nihon Univ. Hosp., Tokyo)

Tay-Sachs disease is a genetic disease which is characterized by the accumulation of GM₂ ganglioside in the brain due to the deficiency of hexosaminidase A activity. The disorder is fatal and no effective treatment is available. The genetic counseling and prenatal diagnosis have been widely accepted. Recently we had experienced the antenatal diagnosis of the two cases of high risk pregnancies with Tay-Sachs disease.

The hexosaminidase A in cell free amniotic fluid was separated by the method of iso-electric focusing and the activity was measured with an artificial substrate; 4MU-*N*-acetyl-D-glucosaminide. In one case the amniotic fluid had a deficiency of activity of the hexosaminidase "A" component and in the other had both A and B components. After getting the confluent amniotic fibroblasts, hexosaminidase A and B in the cells were separated with heat denaturation procedure and with acrylamide-gel electrophoresis technique, and the activities were measured. The results showed that one fetus was normal and the other was affected.

The diagnosis of the first case was confirmed normal by the measuring of serum hexosaminidase A after her birth. The pregnancy of second case was terminated, and the diagnosis was confirmed by study of the aborted fetus. Virtually we found the deficiency of hexosaminidase A activity in the brain and liver of the aborted fetus, and also the accumulation of GM₂ ganglioside in the brain.

Measurement of hexosaminidase A activity in amniotic fluid was found to be a reliable

diagnostic procedure, and was a beneficial way to get early information before confirming the diagnosis with amniotic fibroblasts.

A10. Genetic Study in a Family with Argininemia: Makoto YOSHINO, Kaoru KUBO-TA and Fumio YAMASHITA (Dept. Pediat., Kurume Univ., Kurume)

Argininemia is a rare inborn error of arginine metabolism due to a congenital deficiency of arginase. The present paper deals with genetic study in a family with this disease. The proband was a 4 year-old girl with mental retardation, microcephaly and spastic quadriplegia. The concentrations of arginine in plasma ranged from 3.1 to 19.4 mg/dl. The activities of arginase in red blood cells (RBC) were less than 1% of the normal mean for the proband, 26% for father, 33% in mother and 19% in paternal grandfather. An arginine loading test (100 mg/kg, p.o.) revealed a marked delay in the clearance of the amino acid from plasma in the patient, suggesting that the deficiency of arginase was not confined to RBC but it was generalized. The rate of clearance of arginine was significantly slower in mother but it was indistinguishable from those of control in father. The concentrations of arginine in the fasting plasma specimens tended to be higher in the family members with reduced activities of arginase in RBC than in the family members with normal activities or in control. The concentration of arginine in RBC was significantly increased in the proband, and more than 2SD of the normal mean in mother, but it was within the normal range in father. The measurements of concentrations of arginine in plasma and RBC may be helpful in the diagnosis of heterozygosity for this disease when a single enzyme assay using RBC fails to confirm the diagnosis and the results presented were consistent with autosomal recessive mode of inheritance. This patient was the first confirmed case with argininemia in oriental races.

A11. Effects of Enzyme Inhibitors on the Liver Catalase of Mutant Mice: Yukinori SATO, Junko MIZUGAKI and Masana OGATA (Dept. Public Health, Okayama Univ., Okayama)

Homogenates of mouse liver with isotonic sucrose solution were separated by the cell fractionation with repeating centrifugation and the supernatants were used for the inhibition test by the reagents such as 3,5-diiodosalicylic acid lithium salt (LIS), guanidine and azide, heat, acid and alkali. After various treatments, the remaining catalase activities were measured and showed as a relative enzyme activity. Stability of catalase in liver supernatants was compared normal (C3H/Cs^a) and mutant mice which were designated acatalasemia (C3H/Cs^b) and hypocatalasemia (C3H/Cs^c). In both treatments of LIS and guanidine, Cs^a was most stable, and Cs^c and Cs^b were unstable in this order. On the contrary in azide treatment, Cs^b was most stable, and Cs^c and Cs^a were unstable in this

order. After incubation at various temperatures changing from 30°C to 60°C for 10 min, Cs^a was most stable, and Cs^c and Cs^b were unstable in this order. After acid and alkali treatments, relative activities of Cs^c was similar to that of Cs^a in the range of pH 5.5 to 9.0, but Cs^b was less stable than Cs^a and Cs^c in the same range. It is considered that the structure of catalase molecule in liver is different between normal and mutant mice with regard to LIS, guanidine, heat and pH treatments which damage protein tertiary structure affect on the catalase molecule to inactive, but azide which attach to the heme portion of the catalase molecule incompletely inactive catalase.

A12. Catalase Fractions Separated from Acatalasemia Erythrocytes by Chromatofocusing: Junko MIZUGAKI and Masana OGATA (Dept. Public Health, Okayama Univ., Okayama)

When freshly prepared hemolysates of normal, hypocatalasemia and acatalasemia erythrocytes were separated by agarose isoelectric focusing, at least two kinds of isoenzyme of catalase (*pI* 5.3 and 5.9) were shown by detection of enzyme activity and protein and the indirect measurement of pH by eluting method. For preparation of sufficient amounts of catalase isoenzymes in erythrocytes, normal and acatalasemia hemolysates were separated by chromatofocusing in the range of pH 6.8 to 5.0 with Polybuffer 74 and Polybuffer exchanger 94 at 25°C. Eluting conditions were as follows: Column, C10/40; bed height, 36 cm; start buffer, 0.025 M imidazole-HCl, pH 6.8; eluent solution, Polybuffer 74-HCl, pH 5.0; and flow rate, 36 cm/hr. Eluting patterns of protein measured absorbance at 595 nm in acatalasemia hemolysate were similar to those of normal hemolysate. Catalase active fractions were eluted in the range of pH 6.5 to 5.8 (fraction number 16 to 60) in acatalasemia and normal hemolysates by the titration method. When catalase active fractions were concentrated with Amicon and analyzed by agarose isoelectric focusing, catalase bands were focused at pH 6.2 and 4.9 by the direct measurement of pH with electrode. When catalase fractions of normal hemolysate were analyzed by SDS-PAGE, number 18 to 44 gave two protein bands; one with a molecular weight (MW) of about 60,000 corresponding to the catalase subunit, and the other with a MW of about 30,000. Numbers of 16 to 20 and 39 of catalase fractions of acatalasemia hemolysate gave two protein bands similar to these of normal, number 24 to 35 gave one band with a MW of about 30,000 and number 42 to 44 gave one band with a MW of about 60,000 by SDS-PAGE. Catalase fractions of normal hemolysate (No. 18-44) reacted with anti human erythrocyte catalase IgG and those of acatalasemia hemolysate (No. 16-24) reacted with this antibody by double immunodiffusion test.

A13. Hereditary Persistence of Fetal Hemoglobin (HPFH) Tokushima Variant. Uneven Distribution of HbF among Red Cells: Kiyoshi HASEGAWA, Hisaomi KAWAI, Yoshikado KANETO, Shinji NIKI (Dept. Int. Med., Tokushima Univ., Tokushima), Toshinao YAMANO (Dept. Int. Med., Kochi Med. Sch., Kochi) and Kazuo MIYOSHI (Dept. Int. Med., Tokushima Univ., Tokushima, Okinaka Mem. Inst. Med. Res., Tokyo)

It was discovered previously (1977) in our laboratory that hereditary persistence of fetal hemoglobin (HPFH) Tokushima variant was found in as high as 10% of males and 19% of females among healthy adult Japanese and was inherited as an X-linked dominant trait. This HPFH displayed F-cell % of $8.4 \pm 2.7\%$ (mean $\pm$ SD) and HbF content of $1.40 \pm 0.63\%$ (mean $\pm$ SD). In the present paper, uneven distribution of HbF among red blood cells of this HPFH was reported.

Indirect immunofluorescent antibody technique was employed to stain HbF in blood smears. Two hundred blood cells per preparation were studied by microspectrophotometry to determine the intensity of fluorescence of HbF in each cell, expressed as arbitrary unit (AU).

Distribution of HbF in red cells from cord blood (8 cases, F-cell ranged 96–99%) made one group of 15.0 ± 2.8 AU (mean $\pm$ SD), fusiform in appearance. By contrast, HPFH (10 cases) and non HPFH (8 cases) displayed two groups, the major HbF-low group and the minor HbF-high group by using 0.5 AU as a dividing point. The percentage of the latter averaged about 30% in HPFH and about 10% in non HPFH. HbF-high groups showed HbF content of 2.7 ± 2.3 AU and 1.4 ± 1.3 AU (mean $\pm$ SD) in HPFH and non HPFH, respectively. HbF-low groups gave values of 0.2 ± 0.1 AU (mean $\pm$ SD) in both.

Thus, the distribution of HbF among red blood cells of HPFH Tokushima variant was shown to be uneven, because the red blood cells could be divided into two groups of HbF content, HbF-low and HbF-high groups, and because the HbF distribution among the cells of both groups was dispersed, in contrast to that of cord blood. HPFH Tokushima variant might well have a defect at a genetic level in switching of HbF to HbA, which stopped a little short of complete conversion to adult type.

References: 1) Miyoshi, K. *et al.* 1977. *Igagu No Ayumi*, **103**: 146. 2) Miyoshi, K. *et al.* 1978. *Jpn. J. Human. Genet.* **23**: 264. 3) Miyoshi, K. *et al.* 1979. *Jpn. J. Med.* **18**: 183.

A14. Hb Matsuyama ($\alpha_2^{16\text{Lys} \rightarrow \text{Glu}}\beta_2$) Identical as Hb I First Discovered in Matsuyama: Shuji SAITO, Shigeru FUJITA and Yoshiro OHTA (1st Dept. Med., Ehime Univ. Sch. Med., Ehime)

An electrophoretically fast moving hemoglobin was detected by the hemoglobinopathy survey in Ehime prefecture. Propositus was a 48-year-old woman. Abnormal component was isolated on CM-cellulose column chromatography and its content was about

15%. Chain separation of this abnormal component was revealed α -chain abnormality. Isolated abnormal α -chain was subjected to aminoethylation, tryptic digestion and peptide mapping. On the peptide map, normal α Tp3 and α Tp4 were missing, and a new peptide was observed on more anodal area of normal α Tp4.

Amino acid analysis of this new peptide revealed that a glutamic acid was substituted for the usual lysine at the 16 position of the α -chain. We concluded that this variant is identical with Hb I, but our case is the first one of Hb I discovered in Japan.

A15. Hb Yawatahama ($\alpha_2\beta_2$ 77 His $\rightarrow$ Asp) Identical as Hb J Iran First Discovered in Ehime, Japan; Shigeru FUJITA, Shuji SAITO and Yoshiro OHTA (1st Dept. Med., Ehime Univ. Sch. Med., Ehime)

A fast moving abnormal hemoglobin (Hb Yawatahama) was detected on starch-gel electrophoresis at pH 8.6 of hemolysate of 26 years old female. Abnormal hemoglobin was isolated on CM-cellulose column chromatography with pH gradient of 0.01 M sodium phosphate buffer containing 0.01% KCN. Content of abnormal hemoglobin, Hb A and Hb A₂ were 44%, 53% and 3% respectively. Chain separation of purified abnormal hemoglobin on CM-cellulose column chromatography with concentration gradient of sodium phosphate containing 8 M urea and 0.05 M 2-mercaptoethanol revealed β -chain abnormality. Isolated abnormal β -chain was subjected to aminoethylation, tryptic digestion and peptide mapping. On the peptide map, normal Tp-IX was missing and new peptide was observed on more anodal area than normal Tp-IX, near Tp-V. Amino acid analysis of this new peptide revealed that the peptide was composed of 16 amino acids, including 4 aspartic residues and no histidinyl residue compared with 3 aspartic residues and one histidine of normal β Tp-IX. This data concluded that histidinyl residue at β 77 was replaced by aspartic acid in Hb Yawatahama.

This amino acid substitution was already reported as Hb J Iran by S. Rahbar *et al.* in 1967. Our case was the first one of Hb J Iran discovered in Japan. This abnormal hemoglobin caused no hematological abnormalities in heterozygotes for this hemoglobin as reported before. In our case, the abnormal hemoglobin was not detected in parents and sister of the proband. The explanation for this, whether or not mutation occurred in proband, has not been clear.

- A16. Hb G Szuhu [$\alpha 80$ (EF-4) Asn $\rightarrow$ Lys]. A Hemoglobin Variant Discovered by the Hemoglobinopathy Survey in Takamatsu District: Shunichi SHIMASAKI, Iwao IUCHI, Kazuo HIDAKA, Teruo HARANO, Satoshi UEDA (Dept. Biochem., Int. Med., Kawasaki Med. Sch., Kurashiki), Jun MIZUSHIMA (Kurashiki Cent. Hosp., Kurashiki) and Kiyomi KAWADA (Kagawa Prefect. Cent. Hosp., Takamatsu)**

An electrophoretically slow moving hemoglobin variant was discovered by the hemoglobinopathy survey in Takamatsu district. The propositus was a 24-yr-old pregnant female who was admitted to the Kagawa Prefectural Central Hospital for her delivery.

No hematological abnormality which might be associated with this hemoglobin was seen at the time of admission. The proportion of abnormal hemoglobin (=Hb X) was 42.2% (Hb A=54.7, Hb A₂=3.0, Hb F=0.13). This variant revealed neither instability nor significant change in oxygen affinity. The absorption spectra of the purified Hb X were identical with those of Hb A over the UV and VIS wave length region.

The primary structure of this abnormal hemoglobin was verified as $\beta 80$ Asn $\rightarrow$ Lys replacement by our well established technics. Accordingly, the variant was identical with Hb G Szuhu which was reported at first in a Chinese family in 1961 and then in three Japanese families. No blood relationship among these Japanese families was proved after careful inquiry with the family members.

- A17. Hemoglobin J Lome. Beta 59 (E3) Lysine $\rightarrow$ Asparagine: Jun SUGIHARA, Takashi IMAMURA, Toshikazu MATSUO, Masaaki KAGIMOTO, Ikuo SUMIDA and Toshiyuki YANASE (1st Dept. Med., Kyushu Univ., Fukuoka)**

Hemoglobin J Lome, in which an asparagine residue is substituted for a lysine at position 59 of the β -chain, was detected in a Japanese family. The proposita was a 53-year-old woman. Hematological data and peripheral blood morphology were normal. The isopropanol test was negative for unstable hemoglobin. The variant hemoglobin migrated faster than Hb A on thin-layer starch gel at pH 8.6. The hemoglobin fractions were separated on DE52 chromatography by the method previously described. Hemoglobins J Lome, A, F, and A₂ comprised 43.2%, 52.2%, 1.2% and 3.4% of the total, respectively. The abnormal movement of the β -chains on CM52 column chromatography suggested that the abnormality was in the β -chains. The nature of the amino acid substitution was examined by the two-dimensional peptide mapping of the tryptic digest of non-derivatized globins. It was apparent that the normal tryptic peptide, β T6, was absent. All peptides were analyzed for amino acid composition. These results and the known enzymatic specificity of trypsin indicated that a lysine residue was replaced by an asparagine at position

59 of the β -chain. Oxygen equilibrium curve of Hb J Lome was identical with that of Hb A at pH 7.4 and 37°C.

A18. Study of Two New Electrophoretically Detected Variants of Triose Phosphate Isomerase from Human Red Blood Cells. I. Discussion of Separation and Purification and Electrophoretic Pattern: Jun-ichi ASAKAWA and Harvey W. MOHRENWEISER (RERF, Hiroshima and Univ. Michigan, U.S.A.)

Triose phosphate isomerase (TPI) of human red blood cells is composed of two polypeptide chains. Three bands showing strong activity and several bands showing weak activity are observed upon staining after starch gel electrophoresis using a pH 7.4 buffer containing 0.1 M Tris, 0.1 M maleic acid, 0.01 M EDTA, and 0.01 M $MgCl_2$. In electrophoresis using the above-described buffer, the variant TPI Manchester found in American whites has cathodal migration and the variant TPI 3 HIR 1 found in Hiroshima residents has anodal migration. After phosphocellulose chromatography, ammonium sulfate fractionation and DEAE cellulose chromatography of one normal type and two variant type erythrocyte TPIs, isozyme bands were separated and purified by means of polyacrylamide gel electrophoresis. These isozymes, after their dissociation in a 0.1 M Tris-HCl buffer of pH 7.6, containing 0.1 M mercaptoethanol and 8 M urea, were reassociated by dialysis against a 0.01 M mercaptoethanol, 0.1 M Tris-HCl buffer of pH 7.6. By dissociation and reassociation between normal and variant type isozymes and analysis of their electrophoretic patterns, a conclusion was derived which strongly supported the report of Gracy *et al.*¹⁾ That is, the two polypeptide chains constituting the TPI are the same, each having two labile asparagin residues (Asn 15, Asn 71), with deamidation occurring alternately in the pair of polypeptide chains. It is probably as a result of this that several isozyme bands are shown in electrophoresis.

Reference: 1) Gracy R.W. et al. 1980. *Fed Proc.* 39, 1960.

A19. Study of Two New Electrophoretically Detected Variants of Triose Phosphate Isomerase from Human Red Blood Cells. II. Stability, Kinetics and Immunological Properties: Jun-ichi ASAKAWA and Harvey W. MOHRENWEISER (RERF, Hiroshima and Univ. Michigan, U.S.A.)

The electrophoretic variants TPI 1—Manchester and TPI 1-3 HIR 1 had the same activity in hemolysate as normal type isozymes. Isozyme bands were separated and purified by the method described in the previous report and comparison was made with the normal type regarding their stability, kinetics and immunological properties. Enzyme activity was measured by Gracy's method¹⁾ using a miniature fast analyzer, with glyceraldehyde-3-phosphate (GAP) as substrate. No differences were observed in the K_m values for GAP and

dihydroxy-acetonephosphate nor in the inhibition by substrate-like compounds. Study of stability in buffers of pH 2–11 revealed no difference, the normal type and the variant types both being stable at pH 6–10, nor any difference in denaturation in tests using guanidine-HCl and urea. On the other hand, in heat denaturation tests, to lose 50% activity normal type isozymes required 26 min at 55°C and 15 min at 57°C, but TPI Manchester required 16 min and 9 min, respectively, showing instability. TPI 3 HIR 1 showed no difference from the normal type. To determine their immunological properties, the antiserum obtained by immunizing chicken with purified human TPI isozymes was incubated with each isozyme and the residual activity of the supernatant obtained after centrifugation was measured. Whereas the residual activity of the normal type and TPI Manchester was 10%, TPI 3 HIR 1 showed a high residual reactivity of 35%, with a low reactivity to anti-serum. This suggests that amino acid substitution in TPI 3 HIR 1 occurs at a point where some change is brought about in the antigen antibody reaction.

Reference: 1) Gracy R.W. 1975. *Methods in Enzymol.* **41**, 422.

A20. Overproduction of Structurally Normal Enzyme in Man—Hereditary Hemolytic Anemia with Increased Red Cell Adenosine Deaminase Activity: Hisaichi FUJII, Kenzaburo TANI and Shiro MIWA (Dept. Med., Inst. Med. Sci., Univ. Tokyo, Tokyo)

We discovered a case of hereditary hemolytic anemia due to 40-fold increase in activity of red cell adenosine deaminase (ADA). We purified normal and the patient's enzymes using antibody affinity chromatography, and could not find any apparent abnormality of the enzyme molecule. Therefore, the increased activity of enzyme appears to be caused by the increased concentration of enzyme in the patient's red cells. The increased concentration must be caused either by the increased synthesis of precursors of red cells, or by the prolonged decay of ADA during the life of the red cell. We examined the rate of synthesis and degradation of ADA.

Normal and the patient's red cells were fractionated by centrifugation. There was no significant difference in ADA activity between the normal younger and the normal older cells whereas decreased ADA activity of the patient's red cells was noted in cell-aging. Erythroid colony cell culture was carried out essentially according to the methylcellulose technique described by Iscove *et al.* On day 14 after the initiation of the culture, each plate was incubated with [³H]leucine. After 24 hr of radioactive labeling, isotope-labeled ADA was purified by a specific immunoprecipitation and SDS-polyacrylamide gel electrophoresis. Rate of ADA synthesis in erythroid colony cells cultured from the patient's bone marrow cells was 11.1-fold greater than that from the normal.

It is apparent that the increased number of the enzyme molecules is not subject to pro-

longed decay of ADA in his red cells. Isotope incorporation studies confirm that erythroid colony cells from the patient's bone marrow synthesized much more ADA than those from the normal. The precise mechanism of this abnormality remains unknown, but it may be a defect in which mutation at a control gene results in increased rate of synthesis of ADA of normal structure.

A21. Deficiency of Adenine Phosphoribosyltransferase (APRT): Zen-ichi OGITA, Masa-haru ISOBE (Dept. Biochem. Pathol., Inst. Orient. Med., Toyama Med. Pharma. Univ., Toyama), **Takao OSADA** (Dept. Urol., St. Marianna Univ., Kawasaki), **Yasuo HASHINAKA and Takanobu FUKUNISHI** (Hyogo Prefect. Nishinomiya Hosp., Nishinomiya)

We studied the clinical and biochemical manifestation of partial or complete adenine phosphoribosyltransferase (APRT) deficiencies in two different cases. Case 1: A 46-year-old male patient who had recurrently urinary calculi of 2,8-dihydroxyadenine was presented. When enzymatic examination of hypoxanthine-guanine phosphoribosyltransferase (HPRT) and APRT in his erythrocyte and his hair roots was carried out by electrophoretic method, we could not detect the APRT activity. Case 2: A 33-year-old male who had urolithiasis due to partial deficiency of APRT was presented. APRT activities in erythrocyte of propositus, his clinically normal brother and mother were 72%, 20% and 43% of normal activity respectively. Erythrocytes APRT of propositus, his brother and mother had the same mobility as normal control. These results suggest that these members are all heterozygotes, and the relationship between urolithiasis and APRT activity is affected by environmental factor and other factors.

A22. X線のマウス雌生殖細胞処理による転座個体誘発の可能性について：田中憲穂・加藤基恵・岩原繁雄 (食品薬品安全センター・秦野研究所・遺伝). **Possibility of the Heritable Translocation Inductions by X-Ray in Female Mice: Noriho TANAKA, Motoe KATOH and Shigeo IWAHARA** (Genet., FDSC, Kanagawa)

哺乳動物の雌生殖細胞は、化学物質や放射線などの変異原に対して抵抗性を示す。その理由の一つとして、卵細胞は出生後から排卵直前まで複糸期で休止しており、その間、修復機構が十分に働いていることによるといわれている。本実験では、マウス成熟卵子期に X 線を急照射することにより、F₁ での転座個体誘発の可能性を調べ、DNA に対し多様な反応性と蓄積効果を示す化学物質の場合とのその生成機序の相違について検討した。X 線は、100R または 300R (90R/min) を排卵推定時刻の 6 時間前、12 時間前、18 時間前の各時期に照射した。その結果、排卵 6 時間前において、300R 照射群では 100%、100R 照射群では約 60% の優性致死率 (DL) を示し、この時期が化学物質の場合と同様に染色体異常誘発に高い感受性を示した。一方、排卵 12 時間および 18 時間前ではそれぞれ 10.3% と 14.4% の DL を示した。F₁ での転座誘発に関しては、妊性試験の結果では排卵 6 時間前が約 9% と高い値を示した。

以上の結果は、X 線により生じた排卵直前の傷害は大部分が未修復のまま染色体異常を形成し、一部受精後の前核で修復されることを示唆している。

A23. X-Chromosome Inactivation in the Embryonic Ectoderm from Early Female Mouse Embryos: Nobuo TAKAGI (Chromosome Res. Unit, Fac. Sci., Hokkaido Univ., Sapporo)

By means of a BrdU labeling-acridine orange fluorescence staining technique, we studied chronology of X-chromosome replication in female mouse embryos with two morphologically distinguishable X-chromosomes at early post-implantation stages. Our observation showed unequivocal regionalization of the embryo with respect to the temporal appearance, parental origin, and DNA replication behavior of the allocyclic X-chromosome: The majority of embryonic ectoderm cells at 5.3-days of development had two isocyclic X-chromosomes, while virtually all extra-embryonic cells contained an early-replicating, paternally-derived X-chromosome. By about 6 days of gestation, this early-replicating X-chromosome had changed into a late-replicator in the extra-embryonic ectoderm and proximal endoderm, but no such switch was detected in the cells of the ectoplacental cone. In the embryonic ectoderm the maternally-derived or paternally-derived X chromosome became late-replicating with equal likelihood between 5.8 and 6.3 days of gestation in the absence of an initial phase of early replication. Since this specific pattern of X-chromosome replication is consistent with the biochemically assessed X-chromosome activity reported in each tissue, we may conclude that there is a close temporal relationship between the cytogenetic and biochemical manifestations of the X-chromosome inactivation process. Furthermore, our findings suggest that there may be some differences in the mechanism by which X-inactivation occurs between the embryonic ectoderm and remaining tissues.

A24. A Study on Staining of Chelate Compounds to Human Chromosome Samples: Kohichi MAMBA, Naoko ITO, Kazuyuki TANIGUCHI, Morihisa SAGI, Yasuhiro KUWAKI, Naomi WATANABE, Mutsuo KITAHAMA (Dept. Leg. Med., St. Marianna Univ. Sch. Med., Kawasaki) and **Akira UCHIUMI** (Natl. Chem. Lab. Ind., Tsukuba)

Five kinds of metal chelate compounds, 1-(2-benzoxazolyl)-3-phenyl-5-(4-sulphophenyl) formazane, 1-(2-benzthiazolyl)-3-phenyl-5-(4-sulphophenyl) formazane, 1-(2-benzthiazolyl)-3-(2-sulphophenyl)-5-(4-sulphophenyl) formazane, 1-(2-benzthiazolyl)-3-(2,4-disulphophenyl)-5-(4-sulphophenyl) formazane and 1-(2-benzthiazolyl)-3-(2-benzthiazolyl)-3-(2-sulphophenyl)-5-(4-nitrophenyl) formazane were synthesized and examined about staining affinity to human chromosome samples.

Each chelate compound was combined with nickel very firmly and changed into the stable structure. Metallic element nickel was detected from the chromosome samples stained with the chelate compound by energy dispersive X-ray microanalyzer (EDX) equipped with scanning electron microscope (SEM). 1-(2-Benzthiazolyl)-3-(2-sulphophenyl)-5-(4-nitrophenyl) formazane combined with nickel revealed the best staining affinity to the chromosome samples in the five chelate compounds. The other four chelate compounds combined with nickel were given an indication of the weak reaction to the chromosome samples.

A25. Q-Banding and Sequential Chromomycin A₃/Methyl Green R-Banding: Etsuji OKAMOTO, Kazushi NOMURA and Koso OHAMA (Dept. Obst. Gynec., Hiroshima Univ., Hiroshima)

Chromosomal Q-heteromorphism has been used as a genetic marker in the studies of pathogenesis of hydatidiform moles, ovarian teratomas and triploid abortuses. Sequential acridine orange R-banding is also useful, but it is not so widely used because of the difficulty of the heating treatment (85°C) in this method.

A new R-banding technique with chromomycin A₃/methyl green was first reported by Schweizer (1976). This method does not need a procedure of the heating treatment. So Q-banding and sequential chromomycin A₃/methyl green R-banding have been carried out in our laboratory, and brought a good quality of chromosome heteromorphisms. Methods of this sequential banding are as follows. The chromosome preparation is stained with 0.005% quinacrine mustard and photographed on Kodak Plus-X film. After destaining with methanol : acetic acid (3 vol/1 vol) the slide is stained with chromomycin A₃ (Calbiochem; 1 mg/1.6 ml phosphate buffer) for 10 min and the slide is rinsed and counterstained with methyl green (Eastman Kodak; 2.6 mg in 50 ml NaCl/Hepes buffer) for 10 min. The slide is rinsed with NaCl/Hepes buffer, mounted in glycerol and coverslipped. The chromosomes are rephotographed on Kodak Plus-X film.

A26. High-Resolution Banding by Treating Cells with Acridine Orange before Fixation: Takako MATSUBARA and Yasuo NAKAGOME (Dept. Hum. Genet., Natl. Inst. Genet., Mishima)

An easy technique of high-resolution banding is urgently needed to know details of chromosome structure and to detect minute chromosome changes. Yunis *et al.* (1976, 1978 and 1981) developed a technique using cell synchronization with amethopterin. Some chemical agents (actinomycin D, BUdR, Hoechst-33258 *etc.*) were also used in culture before fixation and they prevented condensation of some specific segments of chromosomes. Ikeuchi and Sasaki (1979) used ethidium bromide for high-resolution banding.

We present a technique of high-resolution banding by treating cells with acridine orange

before fixation. It has been known that acridine and related compounds bind to DNA through intercalation between normally neighboring base pairs in a plane perpendicular to the helix axis.

The method is very simple: colcemid (0.025 $\mu\text{g/ml}$) was added to the standard blood culture, one hour prior to harvest. Thirty minutes later, acridine orange (20–25 $\mu\text{g/ml}$, 37°C) was further added. The procedure of harvest was as usual except for longer hypotonic treatment (0.075 M KCl, 20 min). Mitotic indices were depressed but the number of bands observed by the trypsin-G treatment was reached over 850 per haploid set. The majority were in the 400–550 band range per haploid set.

The technique is easy to do, effectual, reproducible and may be useful in clinical cytogenetic laboratories.

A27. The Relationship between the Number of Cell Divisions and the Survival of Cells with Radiation-Induced Chromosome Aberrations by G- and FPG-Staining Methods:
Kazuo OHTAKI, Hachiro SHIMBA and Akio A. AWA (RERF, Hiroshima)

The present study was undertaken to analyze the relationship between the number of *in vitro* cell divisions by FPG staining method and the survival rate of cells with chromosome aberrations, especially so-called stable type (Cs) aberrations identified by G-banding, in cultured lymphocytes irradiated *in vitro* with ^{60}Co -gamma ray at a single dose of 200 rad (60.8 rad/min). Cells were harvested at 43, 48, 54, 60, 66, 72 hr after initiation of culture. Chromosomes were examined first for 1,345 G-banded metaphases. After G-banding analysis the slides were de-stained and processed by the FPG method: stained for 15 min with Hoechst 33258, exposed for 20 min to UV at room temperature. The number of *in vitro* cell divisions was determined by the distribution in the number of densely stained chromatids in any given cell. Cells with aberrant chromosomes were classified into (1) Cu-cells (dicentrics, rings and acentrics), and (2) Cs-cells (reciprocal translocations, inversions and deletions). In 1,345 cells analyzed, the numbers of cells at first, second and third *in vitro* cell division were 836, 419, and 90, respectively. The ratio of Cu- and Cs-cells at the first *in vitro* cell division was 1 : 0.6. The frequencies of Cu-cells in each of first to third cell divisions were 36%, 27%, 16%, respectively. This indicated that the frequency of Cu-cells decreased with increase in the number of cell divisions. In contrast, the frequencies of Cs-cells showed 20%, 22%, 38% in each of first to third *in vitro* mitoses. Above evidence seems to support that the apparent gradual elevation in the frequency of Cs-cells with increasing number of cell divisions is ascribable to the elimination of Cu-cells through successive cell divisions.

- A28. 高精度バンド分析による No. 1 染色体短腕部分欠損例の同定と, *PGMI* および *Rh* 遺伝子座位の regional mapping について: 池内達郎・斉藤深美子・外村 晶 (東医歯大・細胞遺伝), 中嶋八良・岡島道夫 (東医歯大・法医), 川崎千里・根本ハツ子 (都立母子保健院・小児). Identification of an Interstitial Deletion on Chromosome 1p by a High-Resolution Banding Technique: Regional Mapping of *Rh* and *PGMI* Loci: Tatsuro IKEUCHI, Fumiko SAITO, Akira TONOMURA (Dept. Cytogenet., Tokyo Med. Dent. Univ., Tokyo), Hachiro NAKAJIMA, Michio OKAJIMA (Dept. Forensic Med., Tokyo Med. Dent. Univ., Tokyo), Chisato KAWASAKI and Hatsuko NEMOTO (Tokyo Metropol. Matern. Child Health Inst., Tokyo)

症例は、健康な両親(母26歳、父29歳)より未熟児(出生時体重1,415g)として生まれた男児。双胎であったが、第2子は胎内死亡、生後4カ月時の主な身体所見:長頭、鼻背隆起、高狭口蓋、小顎、耳介の低位と変形、四肢の短縮、外性器異常(停留睪丸、尿道下裂)、先天性心疾患。生後12カ月で精神運動発達の著明な遅延を認めた。皮膚紋理検査により、右手第1指と第4指に撓側蹄状紋、両手掌に猿線、両手第5指の中節が短い、左右足紋母子球部の無紋などの特異所見が認められた。

末梢血と皮膚組織の培養により、No. 1 染色体の短腕が短いことが確認された。さらに、末梢血培養に臭化エチジウム前処理を施して作製した標本で G バンドの高精度解析を行った結果、患児の核型は 46,XY,del(1)(p22.1 p32.1) (ISCN 1981 の命名法による)と判明した。両親の核型は正常であった。患児と両親の末梢血を用いて28種の多型性を示す遺伝的マーカーを検査したところ、3種について有意な知見が得られた。すなわち、患児の *PGM1*, *Rh*, および *Tf* の表現型がそれぞれ、a2-a1, CcDee および C2-1 のヘテロ接合であった。このことは、これらの遺伝子座位が 1p22.1→p32.1 には存在していないことを意味する。上記3マーカーのうち、*PGM1* と *Rh* の座位は No. 1 短腕に位置づけられており (HGMS, 1979), 前者の SRO は pter→p32 であるが、*PGM1* については3個の矛盾した SRO (p34→p33, p32 または p31.1→p22.1) が知られている。

本研究により、*Rh* の SRO は p32.1→pter と記載でき、*PGM1* に関する第3番目の SRO は p22.1 の1個の細分化バンドに縮小させることができた。

- A29. Regional Mapping of Human Chromosome 2. Assignment of the Genes for Acid Phosphate, Malate Dehydrogenase and Isocitrate Dehydrogenase to 2pter→q22 and 2q24→q35: Hidetsune OISHI, Tohru ITOH (Dept. Genet., Inst. Develop. Res., Aichi Prefect. Colony, Kasugai), Tsutomu YAMANAKA (Cent. Hosp., Aichi Prefect. Colony, Kasugai) and Masanori KOBAYASHI (Nishio Civic Hosp., Nishio)

The structural gene for isocitrate dehydrogenase (IDH 1) have been mapped to q11 or q32→qter of chromosome 2. In addition, confirmed assignments of genes to short arm of this chromosome were also presented for acid phosphate (ACP 1) and malate dehydrogenase (MDH 1). In the present study, we report two cases with partial monosomy of chromosome 2, whose chromosomes were investigated by the fluorescence and trypsin banding techniques. Isozyme patterns in the red cells of the patients and their parents

were also examined.

The first case, a girl was born July 3, 1974, after 37 weeks of gestation, as the third child of a 25-year-old mother and a 29-year-old father. At birth, the girl weighed 2,570 g and was found to have multiple anomaly. Chromosome constitution of the patient was 46,XX,del(2)(q22q24). The second case, a girl was born Aug. 8, 1978, after 39 weeks of gestation, as the second child of a 26-year-old mother and a 27-year-old father. At birth, the girl weighed 2,030 g and was found to have cleft palate and many minor anomaly. The karyotype of the patient was 46,XX,del(2)(q35). However, their parents had apparently normal chromosome sets.

Electrophoretic patterns of the ACP 1, MDH 1 and IDH 1 loci showed same phenotypes in individuals examined of both cases and their values of relative activity for these enzymes were also almost in normal range. Therefore, it was considered that the genes for these markers were still retained in the chromosomes of these patients.

A30. Regional Mapping of the Human Gene for Mitochondrial NAD-Linked Malate Dehydrogenase to the p13-q22 Region of Chromosome 7: I. Kondo (Dept. Human Genet. Inst. Basic Med. Sci., Univ. Tsukuba), Y. Shimizu, M.A. Behzadian and N. Shimizu (Dept. Cell Develop. Biol., Univ. Arizona, AZ., U.S.A.)

We previously reported that the gene for mitochondrial malate dehydrogenase (MDH 2: EC 1.1.1.37) is mapped to the p22-qter region of human chromosome 7. According as a advance of study for human gene mapping, the determination of small regional locus on chromosomes becomes more and more important for linkage study. For further precise regional mapping of this gene, human fibroblast lines GM 1356, carrying translocation chromosome, t(1;7) (p34;p13) or GM 2068, carrying translocation chromosome t(6;7) (q27; q22), was fused with mouse A9 cells which are deficient in HPRT and APRT using PEG 1,000. Twenty eight primary hybrid clones produced by 4 independent fusion progenies in GMA 1356 series and 7 by 2 independent fusions in GMA 2068 series were isolated in HAT/ouabain medium. To study the expression of MDH 2, the hybrid cell extracts and parental cell extracts were examined by double immunodiffusion method in agar plates using antisera against human placental MDH 2 in which cross-reacted mouse MDH 2 was eliminated by absorbed with mouse A9 cell extracts. To analyse the chromosomal constitution in hybrid clones, the chromosome spreads were stained with a mixture of Hoechst 33258 and quinacrine mustard in McIlvines' citric-phosphate buffer (pH 7.0). According to the synthetic study of expression of MDH 2 and the presence of translocation chromosome 7 in 7 hybrid clones, the locus for MDH 2 can be assigned to the p13-q22 region of human chromosome 7.

A31. Tentative Gene Mapping Based on rbc SOD-1 Activities of Chromosome 21 Syndromes: Hiroshi NAKAI and Keiya TADA (Dept. Pediat., Tohoku Univ., Sendai)

An enhancement of erythrocyte superoxide dismutase-1 (rbc SOD-1) activity of Down syndrome was reported by Sitichiu *et al.* and Sinet *et al.* (1974). A case with a monosomy 21 mosaicism showed a half decrease of the activity (Nakai *et al.*, 1980). These evidences gave a reason for a gene dosage study about rbc SOD-1 of chromosome 21 syndromes, in order to estimate its gene locus.

In this report we compared rbc SOD-1 activities of the monosomy 21 mosaicism, r(21) and several types of Down syndromes (regular, translocation, regular type with an additional translocation, mosaic trisomy 21) to normal controls.

Reviewing some references, the smallest region of overlap (SRO) of the SOD-1 gene locus was suggested to the region (q21.4→q22.1) on the chromosome 21. All of the partial monosomy 21s and r(21) did not show any decrease of the enzyme activity, but all cases showed typical features of an antimongolism. The genes concerning to the antimongolism, therefore, were suggested to locate on a more distal part than the SOD-1 gene locus.

This is an interesting fact because that the smallest region of overlap for features of Down syndrome (21q22.3: Mattei *et al.*, 1981) had a common part with that of the antimongolism (21q22.1→21qter).

**A32. Mitotic Activity and SCE Frequency in Relation to Aging in Human Lymphocytes
In Vitro: Mimako NAKANO and Akio A. AWA (Dept. Clin. Lab., RERF, Hiroshima)**

The aim of this study is to clarify the relationship between aging and (1) sister chromatid exchange (SCE) frequency and (2) proliferating capacity of peripheral blood lymphocytes as measured by mitotic index (MI) and by the distribution in the number of cell cycles *in vitro*.

Blood samples were obtained from 20 males and 20 females in the Genetic Study and in the Adult Health Study samples at RERF, consisting each of 4 different age groups, 10–19, 30–39, 50–59 and 70–79, respectively. Blood cultures were prepared according to the BudR-Hoechst technique, and the culture time employed throughout the study was 76 hr.

The present results showed that the MI seemed to decrease with advancing age in both sexes; $p < 0.05$ for males and $p < 0.01$ for females. The frequencies of metaphases per 10^3 nucleated cells in their first and second *in vitro* mitosis have remained almost constant in all age groups examined, but the frequency of metaphases in the third or advanced cell cycles tended to decrease gradually with increasing age in both sexes. Mean SCE fre-

quencies were 6.83 ± 0.90 and 7.67 ± 2.21 for females and males, respectively, with no statistically significant difference between the sexes. Although there was no increase with increasing age in the SCE frequency among the female as reported previously, there seemed to be a positive correlation of the SCE frequency with age in the male. At present, no definitive interpretation can be made to explain the above discrepancy observed between the two sexes. It may be necessary to further investigate whether there is a higher risk of being exposed to various environmental mutagens both spontaneously and occupationally in the male than in the female, which might be related to an elevated rate of SCE frequency in the male.

A33. 低線量放射線被曝とリンパ球の染色体異常：外村 晶・岸 邦和・斉藤深美子
(東医歯大・難研・細胞遺伝). **Chromosome Aberrations in Lymphocytes Exposed to Low Doses of Radiation: Akira TONOMURA, Kunikazu KISHI and Fumiko SAITO** (Dept. Cytogenet., MRI, Tokyo Med. Dent. Univ., Tokyo)

原子力エネルギーの開発にともなって危惧される低線量放射線のヒトへの遺伝的危険度を推定するための基礎的資料の一つとして、関東と関西地区に居住する健康成人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た。対象者は被曝歴の少ない20歳代から60歳代の男女で、10歳階級別に96名を選定した。また、もっとも被曝歴の少ないと考えられる新生児48名についても調査した。

染色体型異常に関しては、新生児では低く、成人では年齢による出現頻度の差異は認められなかった。一方、染色体型異常、とくに二動原体染色体の出現頻度は年齢の増加とともに増加し、10年ごとの増加率は1万細胞当たり1.7と推定された。わが国の自然放射線を年100ミリレムとすると、1レム当たりの二動原体染色体の増加率は 1.7×10^{-4} と計算される。

この結果は、Evansらが原子力潜水艦基地の従業員（年間許容被曝線量5レム）について調査した1レム当たりの二動原体染色体の出現頻度は 1.4×10^{-4} という結果ときわめてよく一致した。放射線被曝に起因すると考えられている二動原体染色体を指標としたリンパ球染色体の調査は、低線量放射線被曝の鋭敏な物差しとなるものと考えられる。

A34. Estimations of Radiation-induced Mitotic Delay and Chromosome Aberrations of Trisomy-21 Lymphocytes in Culture: K. MORIMOTO, T. KANEKO, K. IJIMA, M. HIGURASHI* and A. KOIZUMI (Dept. Public Health., Fac. Med., Univ. Tokyo, Tokyo, *Dept. Public Health., Yamanashi Med. Coll., Kofu)

Phytohemagglutinin-stimulated lymphocytes from normal humans and patients with Down's syndrome were cultured in medium containing BrdUrd so that cells dividing for the first, second and third or more time after initiation of culture could be distinguished by the differential staining pattern of sister chromatids in FPG-stained slides. When metaphase cells from cultures were examined at intervals from 36 to 72 hr, it was found that the relative numbers of 1st, 2nd and 3rd or subsequent division cells shifted with increasing

culture times, and that the shift occurred 6 hr earlier with trisomy-21 cells than that with normal. It was also shown that gamma-ray irradiation of normal or trisomy-21 cells at G_0 induced a mitotic delay of 1.3 hr/Gy or 2.4 hr/Gy, respectively, which was estimated from a dose dependent change in the distribution of 1st-, 2nd- and 3rd- or more division cells in irradiated and control cultures. These data thus indicate that the trisomic cells proliferate faster by 6 hr than the normal, and that the gamma-ray-induced mitotic delay of the trisomic cells is about twice longer than that of the normal. When 1st division cells were only scored, it was found that the aberration yield of dicentrics and rings in trisomic cells was about 1.6 times higher than that in normal cells. It also appeared that the yield of chromosome-type breaks in trisomic cells was higher than that in normal cells.

A35. Cell Cycle Kinetics and Chromosomal Aberrations in 21-Trisomy Lymphocyte Culture; Combined Effects of Radiation and Chemicals: Tetsuya KANEKO, Akira KOIZUMI, Kanehisa MORIMOTO (Dept. Public Health., Fac. Med., Univ. Tokyo, Tokyo), Kumiko IJIMA (Dept. M.C.H., Fac. Health Sci., Univ. Tokyo, Tokyo) and Makoto HIGURASHI (Dept. Public Health., Yamanashi Med. Coll., Kofu)

Experiments were carried out to examine the combined cytogenetic effect of gamma-ray with 4NQO, a monofunctional agent, or Mitomycin C (MMC), a bifunctional one, in trisomy-21 and normal lymphocytes in culture. Cells were cultured in medium containing one of the chemicals tested and irradiated 16 hr after initiation. When cells were only irradiated, the aberration yields in dicentrics plus rings were about 2-fold higher in trisomic cells than in the normal. Treatment with the chemicals only induced no dicentrics or rings. When cells were treated with gamma-ray and 4NQO or MMC, however, the enhancement in numbers of dicentrics plus rings was observed in the normal cells, but not in the trisomic cells. The amount of enhancement for the exchange-type aberrations in the normal cells were about the same as those in the trisomic.

It is suggested conclusively that the trisomic condition in a cell is responsible for the absence of enhancement in radiation induced chromosome aberration yields by 4NQO or MMC. Two possible mechanisms are supposed as to these phenomena; one is related to DNA and chromosome repair in trisomic cells, and the other is the difference in cell mitotic kinetics between trisomic and normal cells.

- A36. Effects of Bleomycin on Sister Chromatid Exchanges, Cell Cycle Kinetics and Chromosome Aberrations in 21-Trisomy Lymphocytes Culture: Kumiko IIJIMA (Dept. Matern. Child Health, Univ. Tokyo, Tokyo), Kanehisa MORIMOTO, Tetsuya KANAKO, Akira KOIZUMI (Dept. Public Health, Univ. Tokyo, Tokyo) and Makoto HIGURASHI (Dept. Public Health, Yamanashi Med. Sch., Kofu)**

The 21-trisomic lymphocytes from Down syndrome patients are known to show higher susceptibility to chromosome aberration formation by X-rays. Because bleomycin is an X-ray type chemical agent, we have examined the effects of bleomycin on the inductions of sister chromatid exchanges (SCEs), chromosome aberrations and cell cycle delays in normal and 21-trisomic lymphocytes in culture.

The peripheral blood from three Down syndrome patients and three age matched controls were cultured in the medium containing $20 \mu\text{M}$ BUdR. Cells were treated with bleomycin ($20\text{--}100 \mu\text{g/ml}$) for 3 hr at G_0 immediately before adding PHA. Harlequine chromosomes were obtained by the FPG method.

The frequency of dicentrics and rings in cells increased with increasing concentrations of bleomycin; $100 \mu\text{g/ml}$ bleomycin induced the frequencies of 0.90, 0.22, 0.07 in normal controls and 1.62, 0.36, 0.10 in 21-trisomic cells at the first, second and third cell division respectively. Most of the dicentrics in trisomic cells were removed through the first cell division.

The frequency of SCEs increased with increasing concentrations of bleomycin. But there was no significant difference between trisomic cells and normal controls.

- A37. 染色体異常症例から由来した EB ウイルスによるリンパ芽球細胞株の樹立: 池内達郎・山本興太郎・外村 晶 (東医歯大・難研・細胞遺伝). Establishment of Lymphoblast Cell Lines by EB Virus Infection from Patients with Chromosome Abnormality: Tatsuro IKEUCHI, Kohtaro YAMAMOTO and Akira TONOMURA (Dept. Cytogenet., Tokyo Med. Dent. Univ., Tokyo)**

ヒト末梢血リンパ球に Epstein Barr virus (EBV) を感染させると, B 細胞が芽球化し永続的に増殖可能な細胞株が得られる。われわれは, この方法を用いてさまざまな染色体異常症例から由来したリンパ芽球細胞株の樹立を試みている。

0.3~1.5 ml の末梢血から分離したリンパ球を B95-8 細胞 (マーモセット由来) の培養上清 (EBV 添加) 中に懸濁させ 90 分間 37°C で振盪した後, RPMI 1640 培地 (20% FCS 含有) 1 ml 中に移し CO_2 恒温器で培養を開始する。これまでに核型正常例 (染色体異常児の両親, 網膜芽細胞腫患者など) を含めて 28 例について試み, 23 例 (82%) の株化に成功した。株化に要する期間は, 平均 14.9 日であった。株化細胞の増殖はよく (倍加時間: 20 時間前後), RPMI 1640 培地 (7% FCS 添加) 中で培養を継続することができる。また, 液体窒素凍結保存後の再培養も容易である。株化細胞は元の核型を保持し, 樹立後少なくとも 4 カ月以内では染色体変化はみられない。6 カ月以上継代した株の中には, 5~10% の細胞にさまざまな付加的構造異常 (欠失, 転座, 重複など) が観察された例があ

った。染色体異常症例から樹立しえた細胞株は次のとおりで、その一部は症例の確定診断を目的とした精細な染色体検査に供している：1p-；13p-；7q-；1q-；13q+；22p+；t(2;18)；t(1;4;?)；t(1;6;?)；psudic (18)；dup(2)(q23→pter)；XXYY。

本法は、染色体検査の実用面で有効であるばかりでなく、異常核型を有する株細胞は広く体細胞遺伝学の分野でも有用な試料となることが期待される。

A38. Establishment of Unique B-Lymphoid Cell Lines Which Retain Original Characteristics of Quadriradial, Increased SCE in Bloom Syndrome: Yukimasa SHIRAI (Lab. Human Cytogenet., Dept. Anat., Kochi Med. Sch., Kochi)

We have established unique B lymphoid cell lines from four Bloom syndrome (BS) patients using EB virus (EBV). Even though PHA stimulated BS lymphocytes from all five patients showed high levels of SCE with almost no significant difference among them, three EBV-transformed BS-B lymphoid cell lines had normal levels of SCE and two BS-B lymphoid lines each had two lines; one with the original increased SCE and chromosome instability (including breaks and quadriradials), and the other with normal levels of SCE and without structural aberrations. Interestingly, some karyotypically abnormal clones were paralleled with the increased SCE in the two cell lines, which showed 100% abnormal karyotypes consisting of two major clones, respectively. A 14q+ marker chromosome, which was derived from a patient who had had malignant lymphoma, was observed in one of the cell lines. These karyotypic abnormalities were never observed in cells of many long established normal B lymphoid lines transformed by EBV. These findings strongly suggest that these BS-B cell lines with abnormal karyotypes indicate *in vivo* chromosome abnormalities not from *in vitro* effect through transformation by EBV. This new finding, of the coexistence in the blood of one person of an abnormal and normal population of cells with respect to the number of SCE, poses an interesting problem that is difficult to explain in view of the autosomal recessive inheritance of BS.

A39. Complementation Analysis of Bloom's Syndrome by Cell Hybridization: Michiro C. YOSHIDA (Chromosome Res. Unit. Fac. Sci., Hokkaido Univ., Sapporo), Hiroko KAWASHIMA (Dept. Pediat., Sch. Med., Kanazawa Univ., Kanazawa) and Hiroaki TAKAHASHI (Dept. Pediat., Kanazawa Med. Univ., Ishikawa)

Bloom's syndrome (BS) is an autosomal recessive disorder characterized by stunted growth, sun-sensitive facial skin lesion, a defective immune response, an abnormally high risk of cancer, and high frequencies of spontaneous chromosome aberrations and sister chromatid exchange (SCE). These cytogenetical characteristics were used to examine the question of genetic heterogeneity among BS patients by means of cell fusion. If genetic heterogeneity exists, complementation should lead to normal level of the frequencies of

SCE and chromosome aberrations in somatic cell hybrids. Lymphocytes which were separated from heparinized blood from two Japanese BS patients, BS1KA (BS Registry no. 72) and BS2KA (BS Registry no. 86), were fused with polyethylene glycol and cultured for 2–4 days in the presence of PHA and 5-bromodeoxyuride. Cytogenetically hybrid cells appeared to be tetraploid with an Y and three X chromosomes. Hybrid metaphases retained the characteristic high levels of SCE and chromosome aberrations similar to those of tetraploid metaphases of each parental lymphocyte. These results indicate that there is no genetic complementation among the two Japanese BS patients.

A40. Ultraviolet Light-Induced Sister Chromatid Exchanges in Bloom's Syndrome

Skin Fibroblasts: Takayuki KURIHARA, Masao INOUE (Cent. Lab., Kanazawa Med. Univ.), Kouichi TATSUMI (Dept. Med., Kanazawa Med. Univ., Ishikawa), Hiroaki TAKAHASHI, Mashio KITADANI (Dept. Pediat., Kanazawa Med. Univ., Ishikawa) and Hiraku TAKEBE (Radiat. Biol. Cent., Kyoto Univ., Kyoto)

Cells from the patients with Bloom's syndrome (BS) exhibit extremely high frequency of spontaneous SCEs. Furthermore, it has been reported that ultraviolet (UV) light irradiation elicits an inordinate number of induced SCEs. We attempted to characterize further the UV-induced SCEs in BS cells.

No significant difference was observed between BS skin fibroblasts and skin fibroblasts from normal donors in the sensitivity to UV as measured by inactivation of colony forming ability, the capacity of host-cell reactivation of UV-irradiated herpes simplex virus and the amount of unscheduled DNA synthesis following UV irradiation. The rate of semi-conservative DNA synthesis as determined by [³H]thymidine incorporation was inhibited by UV in BS cells to the same extent as in normal cells. However, the frequency of induced SCEs as a function of UV dose was significantly higher in BS cells than in normal cells. On the other hand, much higher frequency of SCEs was observed with excision-incompetent xeroderma cells (XP, group A) for the equivalent doses of UV. To examine the relationship between the frequency of UV-induced SCEs and its cytotoxic effect, we compared UV-induced SCEs as a function of cell survival among BS, XP and normal cells. BS cells exhibited a significantly greater number of SCEs per lethal event than normal cells, while there was no difference in the yield between XP and normal cells.

The above results indicate that not only the excessive number of spontaneous SCEs but also the increased frequency of UV-induced SCEs may reflect the intrinsic abnormalities in BS cells.

- A41. 常染色体 (18)-X 転座の DNA 複製パターン, 特に late replication について:**
 白石行正・田口尚弘 (高知医大・一解剖), 本森良治 (高知県立中央病院・産婦人).
BrdU-33258 Hoechst Analysis of DNA Replication in a Patient with X-18 Reciprocal Translocation: Yukimasa SHIRAISHI, Takahiro TAGUCHI (1-Anat., Kochi Med. Sch., Kochi) and Ryoji MOTOMORI (Obst. Gynec., Kochi Cent. Hosp., Kochi)

原発性無月経, 軽い webbed neck を主訴とする身長 151 cm, 体重 45 kg, 17 歳女性の末梢血染色体分析を行ったところ, 46,X,t(18;X)(q23;q21),del(20)(p12)(q12) からなる核型異常を呈した. Latt *et al.* (1976) によると, 常染色体との転座による構造異常 X 染色体は early replicate し, 正常形態を有する X 染色体が late replicate することが示されている. そこでわれわれも, BrdU-33258Hoechst 法により本症例の DNA late replication pattern について調べた.

患者末梢血 PHA 培養 72 時間目に BrdU(50 μ g/ml) を添加し, 固定前 5, 6, 7, 8 時間ラベルし標本を作成し, 分染法により後期複製パターンを比較したところ, 正常形態を有する X 染色体が常に late replicate し, 構造異常 X 染色体が early replicate することが判明した. 本症例は初診時, 血中 FCS 101.9, LH 50.9 で buccal smear に clear な sex chromatin を呈しており, エステロゲン, プロゲステロン治療により月経出血が始まっており, この点においても興味ある症例と思われる.

- A42. 葉酸を含まない培養液でみられた染色体切断 (site 3p21):** 上原真理子・木田盈四郎・阿部敏明 (帝京大・小児). **Chromosome Gap Observed by Medium without Folic Acid (Site 3p21):** Mariko UEHARA, Mitsushiro KIDA and Toshiaki ABE (Dept. Pediat., Teikyo Univ., Tokyo)

葉酸は, DNA 合成過程で補酵素として必要なものである. この葉酸を含まない Medium 199 を用いて, 小児神経外来患者 20 人のリンパ球を 3 日培養により染色体分析したところ, 3p21 で高頻度に切断を生ずる患者が 2 人認められた. この現象は葉酸を加えた場合には認められず, また fetal calf serum の割合を多くすると増加した. この性質は経時的に 8 カ月追ってもつねに認められたが, 頻度は減少の傾向を示した. したがって, 他に *in vivo* でのなんらかの要因が関与していることも考えられる. 文献によれば, 3p21 はヒト集団でもっとも切断頻度の高い部位といわれているが, その平均頻度には集団における変異が著しい. このことは, 今回の結果から培養条件の差および集団構成の差から生じていると考えられる.

このような 3p21 での特異的な切断現象について, 集団における変異性, および個体内変動をもたらし要因は何か, また葉酸, fetal calf serum などの *in vitro* における要因は, この現象にどのような意味を持っているかが今後の課題である.

- A43. The Distribution of Break Points in Human Structural Rearrangements:** Yasuo NAKAGOME, Takako MATSUBARA (Dept. Hum. Genet., Natl. Inst. Genet., Mishima), Hiroko FUJITA (Dept. Child. Health, Osaka City Univ., Osaka) and Tatsuo ABE (Dept. Int. Med., Kyoto Prefect. Univ., Kyoto)

It is attempted to settle the issue of whether break points are located within light bands or they are at the interfaces between G-dark and G-light bands in patients with structural rearrangements. Three types of rearrangements, inverted duplications, isodicentric and

rings, were studied. Other abnormalities, including rcp, inv, del(interstitial and terminal), and dir dup, were considered less suitable for the present study.

In 5 out of 6 cases of inv dup, a light band was detected at the median plane and the breakage was located within it. Their karyotypes were inv dup(2)(q21→q11.2), inv dup(1)(q44→q32) (2 unrelated cases), inv dup(4)(p16→p15) and inv dup(11)(p15.5→p13). In one case, the breakage was within a dark band, inv dup(7)(q33→q11). In none of them, breakages were at any of interfaces. A case of dir dup had a karyotype dir dup(14)(q24.3→q32.3). In 2 additional cases, dup(5)(p15→?p11) and dup(21)(q11→q22), no further identification of the structure (dir or inv) was possible. In these 3 cases, distinctions between within-band and interface breakages were not possible. The 2nd group of patients consisted of 7 cases with an isodicentric chromosome with one of its centromeres inactivated. In 5 of them, breakages were within a light band. In the remaining 2, they were within a dark band. A case of translocation dicentric showed breakages within a dark and a variable band. Karyotypes were psu dic(9) (q2101), (21)(q22), (X)(p22), (X)(p11), (X)(q22) (2 cases), (X)(q27) and tdc(7; 15)(p21; p11).

Seven cases of ring chromosomes were also examined. Their karyotypes were r(5)(p15q35), r(6)(p25q27), r(9)(p24q34), r(13)(p11q34), r(13)(p1q34), r(17)(p13q25) and r(X)(p22q28). Twelve breakages were in the most distal light band and 2 were in variable bands.

These results are not compatible with the concept that all or most breakages are located at the interface of bands.

A44. Cytogenetic Studies on Acute Leukemia of Childhood—Summary of 28 Cases:

Ryuichi TSUKINO, Hiromitsu OMORI, Tadashi IIZUKA, Kunikazu SHINOHARA, Tadashi ISHII and Michio KOIKE (Dept. Pediat., Wakayama Med. Coll., Wakayama)

Chromosome analyses were carried out on 28 children under 11 years with acute leukemia for these two years (since December '80 to September '81), using bone marrow and/or peripheral blast cells.

The 28 children were classified into 3 groups: group A included 14 cases (11 ALL and 3 AML) of which examination were done at initial diagnosis and started before treatment, group B included 4 ALL of which examination could not be done before treatment but done at the time when relapse occurred, group C included 10 cases (9 ALL and 1 AML) which are in complete remission for two years.

Among the karyotypes of leukemic cells of 18 acute leukemia of group A and B (15 ALL and 3 AML), 14 showed chromosomal abnormalities (78%). Of ALL, 12 out of 15 cases (80%) had abnormal karyotypes. Judging from the clinical courses, prognosis of 4 hyper-

diploid ALL were relatively good, but 5 pseudo-diploid and 1 near-haploid ALL was poor. Of AML, 2 out of 3 had abnormal karyotypes. One female patient with t(8; 21) is now alive at 1 year and 6 months after onset, but t(8; 21), -X died 8 months after onset, and a male patient with normal karyotype died 24 days after onset due to intracranial bleeding.

A45. Three Cases with Unusual Ph¹ Translocation in Chronic Myelocytic Leukemia:

Eiichi YAO, Masako MATSUNAGA, Yu TOMONAGA, Miyuki KUSANO, Kenji NISHINO, Masuko TAGAWA, Michito ICHIMARU (Atomic Dis. Inst., Nagasaki Univ. Sch. Med., Nagasaki) and Shōtarō NERIISHI (Radiat. Effects Res. Found., Nagasaki)

Among 111 Ph¹-positive cases of chronic myelocytic leukemia (CML), G- and Q-banding studies revealed three cases with unusual translocation, one case with simple and two cases with complex Ph¹ translocation. In these cases, chromosomes of PHA-stimulated peripheral lymphocyte were normal male or female karyotypes. The karyotype of the simple Ph¹ translocation was interpreted as: 46,XY,t(17; 22) (17pter→17q25 :: 22q11→22qter; 22pter→22q11 :: 17q25→17qter), which had been reported in 1976 by M. Matsunaga of our laboratory. The karyotype of the complex Ph¹ translocation in one case was interpreted as: 46,XX,t(5; 9; 22) (5pter→5q31 :: 22q11→22qter; 9pter→9q34 :: 5q31→5qter; 22pter→22q11 :: 9q34→9qter) and in other case: 46,XX,t(9; 11; 22) (9qter→9p13 :: 22q11→22qter; 11qter→11p15 :: 9p13→9pter; 22pter→22q11 :: 11p15→11pter). The clinical and hematologic features of these cases were not significantly different from those of CML cases with the standard type of Ph¹ translocation. A review of the literature revealed that unusual Ph¹ translocation occurred with a frequency varying from 2 to 10% of the cases of CML. In this study, the unusual Ph¹ translocation occurred in 2.8% of the Ph¹ positive CML. In complex Ph¹ translocation, a rearrangement involved between three or more chromosomes, invariably including No. 22, usually No. 9, and least one other chromosome. The long arm of chromosome 9 were involved more often than the short arm of chromosome 9. The rearrangement involving the short arm of chromosome 9 was first reported by G. Gahrton *et al.*, in 1977. The karyotype of their case showed a unusual Ph¹ translocation 46,XY,t(9; 11; 22) (22qter→22q12 :: 9pter→9qter :: 11pter→11p13 :: 11p13→11qter; 22pter→22q11). Our case showed a similar complex Ph¹ translocation involving chromosome 9, 11, and 22.

- A46. 胸水中の double Ph¹ 陽性細胞の株が樹立した CML 急性転化の一例：塩見文俊**
(高知県立中央病院・内科), 白石行正 (高知医大・1 解剖). **Establishment of CML Cell Lines with Double Ph¹ from Pleural Effusion:** Fumitoshi SHIOMI (Int. Med., Kochi Cent. Hosp., Kochi) and Yukimasa SHIRAISHI (1-Anat., Kochi Med. Sch., Kochi)

症例は、昭和50年7月に anemia を指摘され鉄剤にて治療を受けいちおう改善したが、昭和52年 CML と診断され、busulphan 内服にて治療を受けた。53年、骨髓染色体検査にて Ph¹ 染色体が確認された。54年、血液所見は Hb11-9g/dl, Ht 39%, RBC 430×10^4 , WBC $8,700$, Th 32.4×10^4 といちおう慢性期を思わせる所見であったが、splenectomy により染色体検査を行ったところ、21細胞中20細胞に Ph¹ 染色体、1細胞に clear な double Ph¹ 染色体が認められた。以後、間欠的に busulphan 治療がなされたが、55年9月発熱、神経痛が生じ Mybl+Pro 9% となり、Vcp 治療を受け一時軽快したが、56年1月頃より、腫瘤形成傾向を認め、また erythroblast の増加、胸水も認められたため胸水染色体検査を行った結果、調べられた42細胞すべてが $2n=52$ からなる clone であり、100% の細胞に double Ph¹ 染色体が認められた。胸水培養を行った結果、2ヵ月後に二つの cell line が得られ、興味あることに両方とも 100% double Ph¹ を有する $2n=52$ からなる clone であった G-バンド分析によると Ph¹ 染色体は No. 9~22 の標準型であったが、他の染色体の付加的数異常があり、original clone との関連でこの点の検索を行う。

以上の所見のように、いちおう慢性期であっても CML では double Ph¹ の有無をチェックすることは重要であり、たとえ低頻度であっても予後を注意する必要があると思われる。

- A47. Near-Haploid Conversion of Ph¹-Positive Chronic Myelocytic Leukemia: Takaki ISHIHARA, Masako MINAMIHISAMATSU** (Div. Radiat. Hazards, Natl. Inst. Radiol. Sci., Chiba) and Sei-ichi KOHNO (Dept. Biol., Fac. Sci., Toho Univ., Funabashi)

We have encountered a case of Ph¹-positive chronic myelocytic leukemia (CML) whose modal chromosome number was converted from 46 to 27 during about a year's follow-up observation.

The patient was a 67-year-old male with typical CML. The chromosome observation was made 8 times in about a year. In the first two observations when the patient was in chronic phase, the cells from both bone marrow and peripheral blood had 46 chromosomes with the standard Ph¹ translocation between #9 and #22 chromosomes. However, in the 3rd sampling about 8½ months after the 2nd sampling, when the patient was in acute transformation, near-haploid conversion was noticed: Cells with only 27 chromosomes were most frequently observed both in bone marrow and in peripheral blood. The near-haploid clone persisted in nearly constant frequency (58.9% in average) in all the following 5 samplings made in about two months including the last sampling immediately before his death.

The karyotype of the near-haploid cells with 27 chromosomes contained only one chromosome for each chromosome group except for #8, #10, #12 and #21 which had two chro-

mosomes, with Y chromosomes being missing. The Ph¹ translocation between #9 and #22 was retained in all the near-haploid cells. Cells with 54 chromosomes which were also observed in a lower frequency (15.6% in average) were found to possess an exact duplicate set of the chromosomes of the cells with 27 chromosomes.

The results of the observations seem to suggest that it is not all of the diploid set of chromosomes but one set genome of chromosomes that are required for the proliferation of CML cells as a minimum viable unit. The finding that the Ph¹ translocation was retained even in the haploid conversion strongly suggests that the Ph¹ translocation must be playing an extremely significant role in the genesis and proliferation of cells in chronic myelocytic leukemia.

A48. A Case Report of Partial Deletion of the Long Arm of the No. 3 Chromosome:

Kazuo ARAI (Dept. Obst. Gynec., Kimitsu Cent. Hosp., Chiba), **Hisashi MATSUKIYO** (Dept. Pediat., Kimitsu Cent. Hosp., Chiba) and **Hiroshi TAKAZAWA** (Dept. Pathol., Kimitsu Cent. Hosp., Chiba)

Since the advent of banding technique, lots of chromosome anomalies have been found. However, reports on anomalies of the long arm of No. 3 chromosome were extremely rare. In this report, a male baby with many congenital anomalies is described. His karyotype was found to be 46,XY,del(3) (pter-q12 :: q22-qter).

His father was 30 years old and his mother, 22 years old. Neither special genetic problems nor congenital anomalies were found in this family. His parents had not received any X-ray irradiation within a year before gestation. The mother had neither contracted any infection nor taken any drugs during pregnancy. The duration of this pregnancy was forty-one weeks. During pregnancy, any preeclamptic signs had not been found. The delivery was uneventfully.

At birth, his body weight was 1,760 g and length was 43.0 cm. He had many anomalies such as hypotelorism, arhinia without proboscis, cleft lip and palate, hirsutism and cryptorchids. CT scans showed low density almost whole area of the brain. Other anomalies found by autopsy were as follows; structural defects of nasal cavity, holoprosencephaly (without olfactory nerves), patent foramen ovale and patent ductus arteriosus. Both tests were found in internal inguinal canal.

Cytological analysis were done. Karyotype of this patient is 46,XY,del(3) (pter-q12 :: q22-qter). Karyotypes of his parents are normal.

A49. Two Cases of Partial 4q Trisomy: Tamiko SHINOHARA (Dept. Hum. Cytogenet., Japan Red Cross Med. Cent., Tokyo), **Yutaka TAKEUCHI** (Neonatal Care Unit, Matsudo Municipal Hosp., Matsudo), **Kazuo WATANABE and Hiroshi AKAMATSU** (Dept. Neonatal, Japan Red Cross Med. Cent., Tokyo)

Case 1: A male infant was born on January 19, 1981, after 42 week-gestational period. He was the first child of healthy parents, after once spontaneous abortion. At birth, the parents aged 23. His birth weight was 2,310 g, his length 45.0 cm and his head circumference 28.0 cm. His clinical features were antimongoloid and small palpebral fissures, large and low-set ears, flat and broad nasal bridge, hare-lip and cleft palate, micrognathia. His skin was thick and rough. His muscles of extremities were hypotonic. He had bilateral talipes valgus and rocker bottom, his toes were overlapping. At 5 months, he could not hold his head, and his physical and mental developments were retarded (DQ=60). The chromosome constitution of patient was 46,XY,-1,+der(1),t(1;4)(q44;q27)mat. The karyotype of his mother was 46,XX,t(1;4)(q44;q27).

Case 2: A male infant was born on February 14, 1981, after 39 week-5 day-gestational period. He was the third child of unrelated and healthy parents, after once spontaneous abortion and once ectopic pregnancy. At birth, his parents aged 37. His birth weight was 3,500 g. He had apathetic peculiar facies with following abnormalities: asymmetric occiput, antimongoloid slanting of the palpebral fissures, hypertelorism, abnormal movements of eyes, malformed and low-set ears, downturned corners of mouth, micrognathia. He had bilateral inguinal hernias and cryptorchidism. His muscles of extremities were hypertonic. At 6 months, he could not hold his head, and his physical and mental developments were retarded (DQ=57). The chromosome constitution of patient was 46,XY,-22,+der(22),t(4;22)(q27;p12)mat. The karyotype of his mother was 46,XX,t(4;22)(q27;p12).

A50. A Case of Partial 16q Trisomy: Katsuki KOMURA, Masami HORI, Kazuhito JUJO, Toyohiko WATANABE, Masazumi IWAHARA, Toshihiro INO, Kenichiro KANEKO (Dept. Pediat., Juntendo Univ. Sch. Med., Tokyo) and **Tamiko SHINOHARA** (Dept. Hum. Cytogenet., Japan Red Cross Med. Cent., Tokyo)

A 6 month old girl was admitted for the evaluation of psychomotor retardation with heart murmur.

She was born by natural delivery, following an uneventful pregnancy, at 41 weeks gestation. She weighted 2,300 g at birth (SFD) but no remarkable problems have occurred in the neonatal period. On physical examination at admission, she was appeared to be a retardated infant physically and mentally with 30-40% of DQ, with a characteristic face with saddle nose, convergent strabismus and bilateral epicanthus. And the following

findings, such as dermatoglyphic abnormality, café au lait spot, hypertrichosis and generalized muscle hypotonia were found as well. Ejection murmur Levine 4/6 at the third intercostal space of LSB, and ECG and echocardiographic investigations suggested Tetralogy of Fallot for a diagnosis of the heart murmur. EEG revealed no abnormality but CT scan demonstrated brain atrophy at bilateral frontal and temporal lobes. Blood and urine screening tests of inborn errors of metabolism were negative.

Chromosome analysis with G- and C-banding by trypsin and alkaline Giemsa techniques from peripheral blood lymphocytes showed chromosome number 46, with the slight elongation of one of the short arm of the No. 8 chromosome: 46,XX,8p+. Her mother had reciprocal balanced translocation Nos. 8 and 16 chromosomes: 46,XX,(8;16)(p23;q22). Chromosome constitution of the patient was 46,XX,-8,+der(8),t(8;16)(p23;q22)mat. Dermatoglyphic studies revealed that there were 4 ulnar loops and 6 whorls, and the atd angles of both palms were 53°. Variations of simian crease were observed on both hands. This report is the first case of partial 16q trisomy in Japan.

A51. A Malformed Newborn with Monosomy 4qter: Takeshi HISATOMI, Yasushi ONOZUKA (Health Insurance Kawasaki), Yoshikazu KUROKI (Kanagawa Child. Med. Cent., Yokohama)

Five cases of monosomy 4qter, identified by banding techniques, have been reported so far. The authors present a malformed newborn with 46,XX,del(4)(q31), the first case in Oriental.

A female infant with birth weight of 2,630 g and stature of 48 cm was born at preterm to a 29-year-old multigravida by Cesarean section because of fetal distress. Gestational age was 37 weeks. There was no family history of congenital malformation or mental retardation, and the parents were not related. No drugs were administered during the early part of pregnancy nor prenatal infections we noticed. At 37 weeks and 5 days of gestation, the mother was administered to Health Insurance Kawasaki Hospital, because of the early rupture. With the diagnosis of fetal distress, Cesarean section was performed. As the Apgar score was low, and severe asphyxia was observed, intensive care with mechanical respiration was administered. But the treatment was not effective and the death occurred at the age of 8 days.

Main clinical features included wide sagittal suture, hypertelorism, epicanthus, short nasal septum causing an upturned nose, maxillary protrusion, micrognathia, midline cleft of the palate, bilateral simian lines, displacement of the toes, pes planus, muscle hypotonia and wide spaced nipples.

She has many clinical features similar to those described in the literature. The fact indicates no racial difference in this condition.

A52. A Case of X-X Translocation Mosaicism: Tomoko HASEGAWA, Reiko TAJI-KA, Kiyomi YAMADA (Div. Genet., Natl. Med. Cent., Tokyo), Miyuki FUJITA, Sanpei MIYAKAWA and Masashi YAMAGUCHI (Dept. Pediat., Natl. Med. Cent. Hosp., Tokyo)

A patient of X chromosomal mosaicism was presented. The patient was born to a 28-year-old, para 1, gravida 1 mother and 34-year-old father. Birth weight was 3,060 g. At the age of 13 years, fever (37–38°C) was noted before menses. Since about 13 years menstrual cycle and its relation to fever have become irregular. At the age of 15 she was admitted to our hospital, because of bleeding for two months. After that time intermittent fever has gone up to 38–39°C. The symptoms could not be improved by medication. Her height was 142.5 cm, weight 44 kg. She had down-turned slanting eye fissures and low posterior hairline, but neither webbed neck nor cubitus valgus nor other stigmata of Turner syndrome were found. Gynecological examination showed a normal female genitalia. The patient had neither mental retardation nor gross malformations. Endocrine functions of serum estrone, estradiol, estriol, progesterone and testosterone were normal. LH levels increased up to 500 mIU/ml, 55.2 mIU/ml, and 367 mIU/ml by three-time LH-RH tests, and FSH levels increased 500, 19.3, and 31.4 mIU/ml. By HMG test estradiol increased up to 481.0 pg/ml. GH and TSH were WNL.

Chromosomal analysis were performed by culture methods using peripheral blood and skin of the patient. Karyotype analysis by G-banding revealed two types of cells; one was 45,X and the another had 46 chromosomes including an unusual large abnormal chromosome. The short arm and the distal portion of the long arm of this abnormal chromosome was very similar to Xq. The proximal portion of the long arm was seemed to be a deleted Xp. Two centromeric heterochromatin spots were demonstrated by C-banding method; one was on the centromeric region and the other was on the long arm. We considered that this abnormal chromosome was derived from a X-X translocation. The break points were tentatively assigned on a centromeric region of an X and on the Xp21.2. Therefore this patient has probably deletion of Xpter→p21.2 and duplication of Xcent→qter. Almost of these abnormal chromosomes showed a late replication pattern. It was found only in 6% of the cells from 2-day blood culture, but was seen in more than 50% of cells analyzed in cultured skin fibroblasts. The mother had normal karyotype.

A53. Ring 18 Mosaicism in Identical Twins: Akira HATA, Yasuyuki SUZUKI, Yoshikazu KUROKI and Ichiro MATSUI (Div. Med. Genet., Kanagawa Child. Med. Cent., Yokohama)

Two cases with r(18)/normal mosaicism were reported in 4-year-old male identical twins. The clinical features of the proband included short stature (–3.7 SD), mental retardation

(D.Q.=27), microcephaly (-3.8 SD), prominent ears with a hypoplastic helix, midface hypoplasia, a carp mouth, an everted lower lip, a flat nasal bridge, wide spaced nipples, a sacral dimple, and the increased frequency of whorl pattern, which were the characteristic manifestations in the r(18) syndrome. The co-twin showed normal phenotype except for large earlobes and a carp mouth. Zygosity determined on the basis of 9 blood types and 5 enzyme types was monozygotic. Cytogenetic study by lymphocyte culture revealed that the proportion of r(18) was 19.7% in the proband and 19.2% in the co-twin. However, in the fibroblast culture the ring was observed in 51% of cells in the proband and 0% in the co-twin. The most plausible explanation for the mechanism of the discrepant phenotype in the twins is as follows. The first step was a monozygotic gametogenesis following ring formation in the proband. The second step was the twin to twin blood transfusion from the proband to the co-twin through placental blood flow, causing the whole body mosaicism in the proband and the blood mosaicism in the co-twin.

A54. Two Female Cases with r(14) Chromosome: Atsushi IESHIMA and Kenzo TAKESHITA (Div. Child Neurol., Tottori Univ., Yonago)

The proposita HT, female, was born to unrelated parents, following 39 weeks of gestation complicated by severe emesis and toxicemia of pregnancy. The birth weight was 2,140 g. She had respiratory distress and feeding difficulty during neonatal period. She developed normally until 16 months of age, when intractable generalized convulsion occurred. Ataxic gait appeared from 8 years old. At 14 years she showed microcephaly (-4 SD), small stature (-1.4 SD), narrow palpebral fissures, high-arched palate, short fifth fingers, mental retardation (2 or 3 year-old level) and dysequilibrium gait without cerebellar signs. EEG showed no abnormality. The chromosome analysis by G-banded and Ag-stain techniques demonstrated 46,XX,r(14) (p13q32). The karyotype of the mother was normal.

The proposita KW, female, was born to unrelated parents, following 38 weeks of gestation and weighting 2,350 g. She developed normally until the age of 8 months, when she had a generalized convulsion. Despite antiepileptic therapy, grand mal convulsions continued and at the age of 11 years changed into atypical absence and astatic seizure. Ataxic gait appeared at 5 years old. At 16 years she showed short stature (-2.7 SD), microcephaly (-4.7 SD), severe mental retardation (2 or 3 year-old level), scoliosis, pes contortus and no minor anomalies. EEG revealed severe abnormalities of diffuse synchronous irregular spike or polyspike-wave. The karyotype was confirmed to be 46,XX,r(14) (p11q32) by G-banded and Ag-stain techniques. The karyotype of the parents was normal.

In the clinical analysis of 13 cases, major clinical features of the cases with r(14) chro-

mosome were female sex (13/13), epilepsy (13/13), mental retardation (12/13) and microcephaly (8/13).

A55. A Case of *de novo* Reciprocal Translocation. 46,XX,t(X; 13) (p11; q11) with Bilateral Retinoblastoma, Multiple Malformations, and Incontinentia Pigmenti: Akira HATA, Yasuyuki SUZUKI, Yoshimitsu FUKUSHIMA and Yoshikazu KUROKI (Div. Med. Genet., Kanagawa Child. Med. Cent., Yokohama)

The proband, weighed 2,300 g at birth after 39 weeks of uneventful gestation, was the second product of 31-year-old mother and 30-year-old father. Her brother was healthy. She was referred to us on account of feeding difficulty and prematurity of the fundi at 15th day of life. Her clinical features were microcephaly (-3.4 SD), round face, protruding upper lip, downturned mouth, short neck, deformed ears, severe developmental delay, somatic growth failure, and incontinentia pigmenti. She suffered from bilateral retinoblastoma and enucleation of right eye was needed in spite of radiotherapy and photo-coagulation.

Chromosomal analysis by G-banding technique revealed that the karyotype of the proband was 46,XX,t(X; 13) (p11; q11) and those of the parents were normal. Intact 13q14 band was confirmed by high resolution banding method. DNA replicating patterns were studied by BrdU treatment and acridine orange staining. In 34.5% (19/55) of cells, der(X) was inactivated and in the rest cells, normal X was inactive. Inactivation of 13q seems to produce the malformations and retinoblastoma in the present case.

A56. Cytogenetic Studies in a Y-to-X Translocation Observed in Three Members of One Family: Kiyomi YAMADA, Shinichiro NANKO*, Susumu HATTORI and Koichiro ISURUGI (Dept. Genet. Urol., Natl. Med. Cent., Tokyo, *Inst. Brain Res., Univ. Tokyo, Tokyo, **3rd Intern. Med., Jikei Univ., Tokyo)**

A family was reported in which the mother and her two sons were carriers of a Y-to-X translocation, der(X)t(X; Y) (p22; q11). All of the three carriers had short stature and disproportion of extremities but otherwise normal phenotype. One of the sons, the propositus, has been affected with schizophrenia. First evidence so far unreported was obtained that male carriers are probably sterile; the both sons aged 26 and 30 years were azoospermic, and the biopsied specimens of their testes had histologic pictures showing spermatogenetic arrest. Steroid sulfatase activities were within the normal male range in skin fibroblasts from the both male carriers. The mother was H-Y positive, and the normal X chromosome was inactivated in the majority of the cells analyzed. Dermatoglyphics of the three carriers was unusual and dissimilar to those of Turner syndrome patients. The clinical and cytogenetic findings in the present study were compared with

those of the previously reported familial cases, and discussion was made on the genetic background causing phenotypic abnormalities in the male and female carriers. A suggestion was made that the gene order on the Xp22 region may be (Xg)-(H-Y)-(STS)-(CGD) from Xpter.

A57. Retinoblastoma in a Boy with a *de novo* Mutation of a 13/18 Translocation:

Tomiko MOTEKI, Yutaka NAKAZATO, Minami OHUCHI (Dept. Pediat., Univ. Tokyo Branch Hosp., Tokyo), **Mari KOMATSU and Kensei MINODA** (Dept. Ophthalmol., Univ. Tokyo Branch Hosp., Tokyo)

In serial cytogenetic examinations of peripheral lymphocytes from retinoblastoma patients, we found a patient of a sporadic bilateral retinoblastoma with a *de novo* 13/18 translocation with their respective breakpoints being at 13q141 and 18q122. The proband (11-month-old boy) is the second child of unrelated healthy parents who had had a normal 3-year-old daughter. There was no family history of retinoblastoma or other anomalies. Both parents were 26 years old at the time of his birth. Birthweight was 2,800 g and height 49.5 cm at term. At 2 months of age, the right leukocoria was noted and ophthalmologic examinations revealed bilateral retinoblastoma (Reese Va on the right and Ia on the left). The right eye enucleation and radiotherapy on the left orbit were done. Histological examination of the tumor showed the rosette type of retinoblastoma. Both psychomotor development and somatic growth were within normal limits. The G-banding (GAG technique) was done on lymphocytes from ethidium bromide pretreatment 2 hr before harvest in order to get the cell population with high proportion of the cells at early mitotic stages (Ikeuchi and Sasaki). The R-bands were obtained using RBG technique. The karyotype was 46,XY,t(13;18)(q14.1;12.2). His parents' cytogenetic examinations were performed on 50 G-banded cells in each and both showed normal karyotypes. His sister was karyotypically normal as well. Ophthalmologic examinations on both his parents and sister showed no abnormalities.

The present case is interesting because of the simultaneous occurrence of a sporadic retinoblastoma and a *de novo* mutation for a 13/18 translocation with the breakpoint on chromosome 13 being at 13q14.1.

A58. 家族性 Robertson 型転座染色体をもつ患者にみられた付加的構造異常について

(第3報): 斎藤深美子・外村 晶 (東医歯大・細胞遺伝). **Structural Instability of a Robertsonian Translocation Chromosome with Ag-Stained Nucleolus Organizer Region. A Further Study:** Fumiko SAITO and Akira TONOMURA (Dept. Cytogenet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

一昨年われわれは、銀染色部位を有する Robertson 型転座染色体をもつ個体のリンパ球で、転座染色体が解離して別の構造異常を起こしている2例について報告した。そのうちの1例(t(14q21q)を

もつ Down 症候群)では、患児のみならず、この転座の保因者である母親および姉のリンパ球でも、関与する染色体はそれぞれ異なるが同様の構造異常を起こしていた。今回、この患児の皮膚の培養細胞を Q 染色法により染色体分析した結果、継代 2 代目で t(14q21q) をもつ細胞が 61.4%, t(14q15q) が 17.8% みられ、それ以外に t(14q21q)+t(13q15q) の二つの Robertson 型転座染色体をもつ細胞が 16.8% 観察された。10 代目では、おのおの 49.5%, 43.6% および 1.5% であった。

一方、皮膚由来の線維芽細胞を用いた昨年の実験結果から、この転座の結合部位が外的要因 (X 線) に対して感受性をもつことが示唆されたが、今回行ったアルキル化剤 (MMS, 0.25 mM; EMS, 4 mM), MMC (0.01 μ g/ml) および H₂O₂ (5, 10, 20 μ M) 処理後 24 時間で固定した線維芽細胞での分析では、そのような感受性はみられなかった。

以上の結果から、この t(14q21q) の結合部位は、X 線に感受性を示して解離し、別の構造異常を起こすが、X 線で誘起されていないような構造異常 (t(14q21q)+t(13q15q)) が皮膚の線維芽細胞にみられることから、これらの異常を生ずる内的要因等、別の原因も考えられる。

A59. Two Cases of 11p13 Deletion Syndrome with Aniridia, Genitourinary Abnormality, Other Malformations, and Decreased Catalase Activity: Yoshimitsu FUKUSHIMA, Norio NIKAWA (Dept. Pediat., Hokkaido Univ. Sch. Med., Sapporo), Naoyuki TANIGUCHI and Susumu IIZUKA (Biochemist. Lab., Cancer Inst., Hokkaido Univ. Sch. Med., Sapporo).

Two unrelated patients with 11p13-syndrome were reported. Patient 1 was a 3-year-old male child and Patient 2 was a 2-month-old female infant. The clinical features common to the two patients included bilateral aniridia, blepharophimosis, nystagmus, malformed ears, micrognathia, genitourinary abnormality (cryptorchidism in Patient 1; hypertrophied labia minor in Patient 2), mental or developmental retardation, and decreased catalase activity in the erythrocytes. These features are those characteristic to the 11p13 deletion syndrome.

High-resolution chromosome bandings were performed with the ethidium bromide technique. The karyotype of Patient 1 was interpreted as 46,XY,del(11)(p12p15), and that of Patient 2 was 46,XX,dir ins(11;2)(p13;q13q23). Although the chromosome abnormality of Patient 2 seemed balanced, it most likely involved a submicroscopic deletion within the band 11p13 because of her clinical features. The decreased activity of catalase also supported the minute deletion, since a locus of the gene for catalase has been assigned to the band 11p13.

- A60. 精神症状と前縦隔腫瘍を合併したクラインフェルター症候群の1例：豊田勝弘・元村直靖・堺 俊明(大阪医大・神経精神), 安田正幸(大阪医大・外科), 堤 重年(済生会茨木病院・神経精神). A Case of Klinefelter Syndrome with Schizophrenia-like Symptoms and Mediastinal Tumor: Katsuhiko TOYODA, Naoyasu MOTOMURA, Toshiaki SAKAI (Dept. Neuropsychiat., Osaka Med. Coll., Takatsuki,) Masayuki YASUDA (Dept. Surg., Osaka Med. Coll., Takatsuki,) and Sigetoshi TSUTSUMI (Dept. Neuropsychiat., Hosp. Saiseikai, Ibaraki)**

従来, Klinefelter 症候群に精神症状を合併した例は数多く報告されているが, さらに腫瘍を伴った例の報告は数少ない。われわれは Klinefelter 症候群に精神症状と前縦隔腫瘍を併発した例を経験したのでここに報告する。

症例は19歳男子。14時, 被害・関係妄想, 思考化声, 幻聴などの病的体験が出現し分裂病の診断のもとに数回入院退院を繰り返す。この間性的倒錯行為を認めている。昭和54年4月ころより咳嗽, 胸部痛出現, 胸部レントゲン写真にて前縦隔に異常陰影を認め, 前縦隔腫瘍と診断され入院となる。入院時, 精神的に幼稚な印象が強く (IQ, 60), 身体的には女性化乳房などいわゆる女性化傾向が著明で, 血中 LH, FSH 高値のほか脳波異常が認められ, karyotype は 47-XXY であった。なお, 前縦隔腫瘍は組織学的には embryonal carcinoma であった。精神症状は昭和54年4月以降認めていなかったが, 術後4カ月目ころより再び被害の内容の幻聴が活発となり, 他患への暴力行為を認めたり, 終始病棟内を徘徊するなど不穏な状態となる。また, 同時に気分の変動がことのほか著しく, 好機嫌な状態と不機嫌な状態とが目まぐるしく変化していた。このような不穏な状態は約4カ月で消退したが, その後も病的体験は引き続き認められる。

- A61. A Case of Cerebral Gigantism with Familial Chromosomal Aberration: Ekuko NAKADA, Makiko OSAWA, Yukio FUKUYAMA (Dept. Pediat., Tokyo Women's Med. Coll., Tokyo) and Tomoko HASEGAWA (Div. Genet., Clin. Res. Inst., Natl. Med. Cent. Hosp., Tokyo)**

A rare chromosomal aberration was detected in a patient with cerebral gigantism and its family members. This findings was considered to be helpful for studying the pathogenesis of the disease. Chief complaint of the patient, a 4-year-old girl, was psychomotor retardation. Clinically, acceleration of growth with advanced bone age and typical physical characteristics—macrocephaly with dolichocephalic tendency, prominent forehead, high arched palate, antimongoloid slant, hypertelorism and pointed chin—were observed. Based on these and other findings including dermatoglyphic and cephalometric studies, the patient was diagnosed as cerebral gigantism. The examination of chromosomes by the Ikeuchi's G-banded method of early metaphase using ethidium bromide revealed pericentric inversion of the 8th chromosome—46,XX inv(8) (p21.3 q22.1). All relatives of the first degree (the parents, non-consanguineous, and an elder brother) were also studied and the same chromosomal abnormality was found in father and brother. Noteworthy was the fact that several dermatoglyphic patterns which were characteristic for cerebral gigantism (the A line terminated at the base of the thumb, palmar alignment tends to be

vertical, the 4th interdigital pattern and the increased total finger ridge count) were observed in the father and brother as well as in the patient. Cephalometry obtained from the brother also revealed the facial findings characteristic for the disease.

According to our extensive review of literature, familial occurrence of this disease has been reported in 13 families including some families showing autosomal dominant inheritance. Normal karyotype was observed in 49 cases by 20 authors, and an extra chromosome in the E group of the mother of one patient and mosaic 46,XY/47,XY,+C in one patient were reported by Milunsky and by Damyanova, respectively. Our case will be the third one in which chromosomal aberration was found.

A62. Cytogenetic and Cytokinetic Effects of Cigarette Smoking on Styrene-Exposed Workers: Toshiaki WATANABE, Akira ENDO (Dept. Hyg. Prev. Med., Yamagata Univ. Sch. Med., Yamagata), Takao WATANABE, Michiko MIYASAKA and Masayuki IKEDA (Dept. Environ. Health, Tohoku Univ. Sch. Med., Sendai)

The rate of sister chromatid exchanges (SCEs) and cell cycle kinetics were examined in cultured lymphocytes of 18 male workers who were occupationally exposed to styrene in FRP (fiber-reinforced plastics) plants. Chromosome preparations were made by the conventional air-drying method and sister chromatids were stained differentially by the modified FPG method. The results were analyzed in relation to cigarette smoking habit of the workers.

In nonsmoking subjects, the SCE rate per metaphase at the 52-hr culture was 7.9 in average for 8 styrene-exposed workers, as compared with the average of 8.6 for 3 non-exposed controls. Whereas, in smoking subjects, the average SCE rate increased to 9.6 in 10 styrene-exposed workers against 8.4 for 3 non-exposed controls. The proportions of M2 (metaphases in the second replication cycle) were 0.25 for smoking controls, and 0.27 and 0.31 for smoking and nonsmoking exposed workers, respectively, which were significantly low than 0.58 of nonsmoking controls. These findings imply that styrene exposure and cigarette smoking affected the DNA replication/repair processes and viability of the lymphocytes and consequently produced such increased SCE rate and delay of cell proliferation *in vitro*. Cigarette smokers had more severe effects of styrene. The effects of organic solvents and cigarette smoking may be synergistic.

- A64. 胞状奇胎細胞の DNA 複製パターンならびに姉妹染色分体交換の研究：白石行正**
(高知医大・一解剖), 塚原正人・梶井 正・今泉 清 (山口大・小児). **Studies on DNA Replication and SCE Hydatidiform Moles.** Yukimasa SHIRAISHI (1-Anat., Kochi Med. Sch. Kochi), Masato TSUKAHARA, Tadashi KAJII and Kiyoshi IMAIZUMI (Dept. Padiat., Yamaguchi Univ. Sch. Med., Ube)

これまでの研究で、胞状奇胎が雄核に由来するホモ接合体であることが指摘されている。すなわち、卵核が排出されるか不活性化をするとともに、ハプロイド精子により受精後、第一卵割期に二倍化する機転である。したがってホモ接合体である完全奇胎における、DNA 複製パターンならびに姉妹染色分体交換 (SCE) の研究は興味あるものである。

われわれは、これまで 5 種類の完全奇胎由来のホモ接合体細胞 (いずれも核型 46, XX) (79M10, 79M16, 80M05, 80M06, 81M02) について調べた結果、BrdU-33258Hoechst 法による DNA 後期複製パターンは、ヒト女性細胞と同じく X 染色体の片方が明らかに late replicate し、同時に常染色体についても相同染色体間で複製にズレが生じることが判明した。SCE に関しては自然発生的にはその頻度は正常範囲であったが、これら 5 種類の細胞はすべてマイトマイシン C (MC) に高感受性であり、正常細胞に SCE を引き起こす約 1/10 濃度で高頻度 SCE を呈し、しかも SCE の相同染色体間における頻度分布は常に不均等に生じており、これらはホモ接合体であるにもかかわらず DNA 複製パターンも相同染色体間でズレているという事実と考え合わせると興味ある所見である。

- A65. 胞状奇胎における染色体の後期複製パターン：塚原正人・今泉 清・梶井 正**
(山口大・小児). **Late Replicating Patterns of Cultured Fibroblasts from Molar Villi:** Masato TSUKAHARA, Kiyoshi IMAIZUMI and Tadashi KAJII (Dept. Pediat., Yamaguchi Univ. Sch. Med., Ube)

完全奇胎 (核型 46, XX・雄核発生によるホモ接合体) 由来培養線維芽細胞、成人皮膚由来培養線維芽細胞に培養最後の 8 時間 BrdU (最終濃度 25 $\mu\text{g}/\text{ml}$)、2 時間コルセミド (最終濃度 0.04 $\mu\text{g}/\text{ml}$) 添加後染色体標本作成。Hoechst 33258-Giemsa 法で染色。おのおの 50 個の染色体を写真分析し、1, 2, 3, 5, 13 番, X 染色体について検討した。1, 2, 3, 5, 13 番染色体はすべて相同染色体間で BrdU 取り込みが中心体付近で同調・非同調の二者がみられ、非同調率は胞状奇胎 16~48%, 成人皮膚 22~54% で両者に差はなかった。X 染色体はすべて非同調性で、後期複製 X 染色体のバンドのパターンは BrdU 取り込み時期の差により少なくとも 5 種類以上あり、また奇胎細胞と成人皮膚ではパターンに微妙な差を認めた。

以上の所見から、完全奇胎はホモ接合体であるにもかかわらず相同染色体間で、1) DNA 後期複製に時間的ずれがある、2) X 染色体の不活性化は母親由来の X 染色体 (完全奇胎の X 染色体は 2 本とも父親由来) が存在しなくても起こりうることを証明した。

B1. Three Recent Cases of Lethal Short-Limbed Dwarfism: Seiji YAMAGUCHI, Tadao ORII, Fumiaki MOTOYOSHI (Dept. Pediat., Gifu Univ. Sch. Med., Gifu), Takuji TANAKA, Shigeo GOTO (1st, 2nd Dept. Pathol., Gifu Univ. Sch. Med., Gifu) and Hideki KACHI (Dept. Pathol., Gifu City Hosp., Gifu)

Lethal short-limbed dwarfism has been attracted attention, and has been classified into eight diseases. We recently experienced three diseases among them.

Case No. 1 was a female infant with campomelic dysplasia. She was stillborn with polyhydramnios at 36 weeks of gestation, and was a micromelic dwarf of body weight 3,140 g and body length 37.0 cm, having a peculiar face. X-ray examination revealed that the long bones were thin bone type, the femur and the tibia were curved and the fibula and the scapula were hypoplastic. Autopsy findings showed the presence of hydrocephalus, pulmonary hypoplasia, urethral atresia and hydronephrosis. There was neither family history of skeletal abnormalities nor consanguinity. A possibility of autosomal recessive inheritance has been recently suspected as to this disease.

Case No. 2 was a male infant with thanatophoric dysplasia. He was born at 34 weeks of gestation complicated with polyhydramnios. His body weight was 2,520 g and his body length was 38.5 cm. He was associated with marked shortend extremities and severe respiratory distress, and died 24 hr after birth. X-ray examination showed thick and shortend long bones, telephone receiver-shaped femur and the flat vertebral bodies. On autopsy, the columnar arrangement of the epiphyseal cartilage cells of femur was irregular. There was neither family history of dwarfism nor consanguinity. In general this disease is known to develop rather sporadically.

Case No. 3 was a male infant with osteogenesis imperfecta, congenital form. His birth weight was 2,558 g, his length was 41.0 cm, and his gestation period was 38 weeks. Membrane-like skull and blue sclera were noted, and X-ray examination revealed multiple bone fractures, and the long bones were thick bone type. He died 39 days after birth because of cardiac insufficiency. His parents were normal, and there was no abnormality of family history. But in general, this disease is known to be inherited by autosomal recessive trait.

B2. Johanson-Blizzard Syndrome in Two Siblings: Akira MATSUI (Dept. Pediat., Isesaki City Hosp., Gunma), Tsutomu TAGUCHI, Kumiko FUGINAGA, Masao TAKEUCHI (Maebashi Red Cross Hosp., Maebashi) and Takenobu KOIZUMI (Dept. Pediat., Sch. Med., Gunma Univ., Maebashi)

Two siblings are presented with Johanson-Blizzard syndrome of aplastic alae nasi, deafness, thyroid dysfunction, dwarfism, absent tooth buds, and malabsorption. Elder sister died of pneumonia at the age of seven months and was found to be complicated with arhinencephaly in addition to many findings usually observed in asplenic syndrome.

Younger sister, two years and ten months of age, had aplasia of alae nasi, deafness, dwarfism, and malabsorption.

The parents are first cousins and were addicted to toluene. The mother had twice induced abortion and one normal abortion between 17 and 19 years old.

One case may be the first report of Johanson-Blizzard syndrome in Japan.

B4. Genetic Investigation of Histidinemic Families: Hiroko YAMAMOTO, Yuko FUKUDA, Yukinobu OHASASA, Yutaka HASE, Tsuneo TSURUHARA (Child. Med. Cent. Osaka City, Osaka), Toshiaki OURA (Sunago Ryoikuen, Hyogo), Harumi OHTAKE, Tomiko FUJIE (Assoc. Environ. Hyg. Osaka City, Osaka) and Shota KAWABE (Dept. Biol., Kobe Univ., Hyogo).

Nail urocanic acid(UA)/histidine(His) ratio was evaluated in the histidinemic patients detected by the newborn screening, their family members and the control subjects. Histidine and urocanic acid were identified on thin-layer chromatograms of the ammonium extract of the nail which developed in butanol-aceton-acetic acid-water solution, stained with Pauly reagent and quantitated by Shimadzu chromatoscanner. Nail UA/His ratio showed a good correlation with stratum corneum histidase activity with the correlation coefficient of 0.76.

In the control subjects, $\log(1 + \text{UA/His})$ of the nail showed normal distribution with its peak between 0.2105 and 0.2605. 97% of the histidinemic patients had their $\log(1 + \text{UA/His})$ less than 0.1105. In the parents, $\log(1 + \text{UA/His})$ distributed in the range of patients and control with its peak between 0.1105 and 0.1605, which was the mean value of the patients and control. Siblings were roughly divided into three groups, namely, patients, control and mean group.

Nail UA/His ratio was not always comparable with the result of histidine loading test. Some parents had normal UA/His ratio in spite of persistently elevated plasma histidine levels after histidine loading, suggestive of heterozygotes of histidinemia.

When the patients and their siblings were evaluated by a priori method, far more histidinemic patients were found than anticipated. It was speculated that some of the parents were not heterozygotes but homozygotes of histidinemia on account of high frequency of histidinemic gene.

B5. Language Delay in Japanese Children: Kenzo TAKESHITA (Dept. Pediat. Neurol., Tottori Univ., Yonago), Reiichiro MAKINO and Goro ANDO (Prefect. Cent. Hosp., Tottori)

Language delay in early childhood is associated with deaf, mental retardation, autistic child and simple developmental speech delay. Estimates of the prevalence of language

delay vary according to the criteria used. In our study, deaf and the diseases with a single clinical entity such as Down's syndrome are excluded. In a total of population of 7,500 three-year-olds carried out in the Tottori prefecture in 1980, it was found that the prevalence was 13.4 per 1,000 children. Criteria of our diagnosis are that they had no meaningful word at their 18 months and they could not joint 2 or 3 words in sentences at three years, or that they were difficult to do over half of the simple tests for communication skills. In 134 children with language delay, 76.3% was in boy. As to the other associated factors, our study found that 26.3% of them had a behavioral problems compared with 1.9% in general. We could not find out the etiological factors in their medical and developmental histories.

B6. 精神分裂病様症状を伴った Pachydermoperiostosis の 1 例：堺 俊明・広沢啓三・米田 博・木戸上洋一（大阪医大・神経精神）. A Case of Pachydermoperiostosis with Schizophrenic Symptoms: Toshiaki SAKAI, Keizou HIROSAWA, Hiroshi YONEDA and Youichi KIDOGAMI (Dept. Neuropsych., Osaka Med. Coll., Takatsuki)

Pachydermoperiostosis は特有な皮膚変化，バチ指，骨変化の三徴候を示し，常染色体性優性遺伝によるといわれている．今回われわれは，分裂病様症状を伴った pachydermoperiostosis の 1 例を経験したので報告し，その精神症状に関して考察を加えた．

症例は 46 歳男子，家族歴には特記すべき負因はない．身体的には，20 歳ころより脳回転状頭皮が出現，その後数年間漸次増強．頭部皮膚の生検により，膠原線維の増生を認めた．骨の L 線検査では指骨，胫骨を中心に骨皮質の肥厚が見られたが，バチ指は認めなかった．血液生化学検査では特記すべき異常は見られなかった．精神症状としては，23 歳ころより病的体験が出現し，消長を繰り返しながらしだいに意欲の減退や bradyphrenia を中心とした．いわゆる分裂病様症状を呈している．

特発性脳回転状頭皮に分裂病様症状を伴った症例の報告は多く，その精神症状は母斑症としての脳回転状頭皮の 1 症状と考えられている．しかし pachydermoperiostosis に分裂病様症状を伴った症例の報告は，本邦において 1 例もない．さて pachydermoperiostosis は，特発性脳回転状頭皮より広範囲の異常を呈する疾患であり，特発性脳回転状頭皮は，pachydermoperiostosis の不全型であるとする考えが有力になっている．すなわち，pachydermoperiostosis も母斑症に属すると考えられ，今回報告した症例における分裂病様症状は，母斑症としての pachydermoperiostosis の症状と考えられる．

B7. The Genetic Study of Familial Amyloid Polyneuropathy in the Arao Focus: Saburo SAKODA, Tomokazu SUZUKI, Sadayoshi HIGA, Masao UEJI, Akira HAYASHI (3rd Dept. Int. Med., Osaka Univ. Hosp., Osaka), Yoshio TAKABA (Arao City Hosp., Kumamoto), Akira NAKAJIMA (Nakajima Med. Clin., Kumamoto) and Norikazu YASUDA (Div. Genet., Natl. Inst. Radiol. Sci., Chiba)

The genealogical survey of familial amyloid polyneuropathy in the Arao focus was done, and the data was analysed statistically. By this survey, 9 families and 91 patients (45

males and 46 females) were found. There was no difference between the sexes. Twenty nine patients are alive (14 males and 15 females). For 44 patients, the mean of onset age was 34.1 years, range 20–46 years. The penetrance due to late onset was 83.5% according to Morton's method. The segregation ratio within 18 sibships in which either parent was affected was $36 \pm 6\%$ for single ascertainment and $46 \pm 5\%$ for complete ascertainment. The corresponding figures within 14 sibships in which neither parent was affected was $30 \pm 7\%$ for single ascertainment and $40 \pm 6\%$ for complete ascertainment. The results of the analysis were thus consistent with the assumption of an autosomal dominant mode of inheritance.

B8. A Family of Sudanophilic Leukodystrophy Presenting Pyramidal Tract Involvement and Presenile Dementia: Satoshi SUZUKI, Takeshi TABIRA, Ikuo GOTO, Yoshigoro KUROIWA (Dept. Neurol., Neurol. Inst., Kyushu Univ., Fukuoka) and Shigemi ANRAKU (Dept. Pathol., Kurume Univ., Kurume)

Familial sudanophilic leukodystrophy of adult onset presenting pyramidal tract signs and presenile dementia was reported. The proband was a 36 y.o. woman who had progressive left hemiparesis and bilateral hyperreflexia in the lower limbs starting at age 35. CT-scan showed diffuse enlargement of ventricles and cerebral atrophy. EEG revealed excessive slowing more on the right. Other laboratory findings including nerve and muscle biopsies were all normal.

Presenile dementia, parkinsonism and gait disturbances were developed in her 3 brothers starting at age about 36 to 45. One of them died at age 40 and the autopsy revealed diffuse demyelination in the cerebral white matter and the pyramidal tracts of the brain stem with sudanophilic granules. The adrenal gland showed focal ballooning of the deep cortical cells but needle-like inclusions were not found. The rapid ACTH test and the analysis of long chain fatty acid in RBC membrane were normal. Hence, adrenoleukodystrophy and adrenomyeloneuropathy were denied. We also ruled out Pekizeus-Merzbacher's disease, membranous lipodystrophy (Nasu-Hakola's disease) and other known metabolic diseases. This is a rare familial sudanophilic leukodystrophy of adult onset with a autosomal recessive trait.

B9. Genetic Mechanism and Counseling of Duchenne Muscular Dystrophy: Kiyotaro KONDO (Dept. Neurol., Tokyo Metropol. Inst. Neurosci., Fuchu) and Norikazu YASUDA (Natl. Inst. Radiat. Res., Chiba)

Duchenne dystrophy is a fatal degeneration of the skeletal muscles inherited X-linked recessively in more than 90% of the Japanese cases, the rest being autosomal-recessive and relatively mild clinically. Genetic analyses with 514 probands disclosed; 1) X-linked

recessive heredity, 2) new sporadic mutants in 1/3 of the cases, 3) equal mutation rate in the ova and the sperms with the estimated value of 6.3×10^{-5} per locus per generation, 4) incidence rate of 21.7×10^{-5} among newborn males and 5) prevalence rate of 5.0×10^{-5} and the estimated total number of the surviving patients of about 2,430 in Japan.

A total of 26 national hospitals provides special programs for schooling and rehabilitation for young victims with neuromuscular diseases, mostly of Duchenne dystrophy. About 1,000 Duchenne patients are being cared in these hospitals. Genetic counseling programs, involving choice of the abortion of male fetuses of heterozygous mothers, are to be organized in close connections with these institutions. Technical problems are being worked out to establish a high-risk registry, with hospitalized patients as the index cases.

B10. 大腸腺腫症における孤発例の検討: 谷村雅子・宇都宮譲二・岩間毅夫(東医歯大・ポリポージス), 小松一太(小松医院). Sporadic Cases in Adenomatosis Coli: Masako TANIMURA, Joji UTSUNOMIYA, Takeo IWAMA (Poliposis cent., Tokyo Med. Dent. Univ., Tokyo) and Ichita KOMATSU (Komatsu Hosp.)

ポリポージスセンターに登録され家系調査を完了した大腸腺腫症 299 家系のデータを用い, 本症孤発例 (124 家系, 41%) の成立理由を検討した. 親罹患家系 108 家系中, 同胞罹患家系 69.5%, 子罹患家系 14.8%, 親非罹患家系 191 家系中, 同胞罹患家系 19.9%, 子罹患家系 18.3% で, 親非罹患家系では同胞罹患が少なかった. 親の親, および親の同胞の罹患有無から本症遺伝子をもっていることが確実な親は 64 名中 60 名死亡, 死亡診断書に記載された死因は大腸腺腫症または大腸癌 66.7%, 消化器系疾患 15.0% で, 他の死因の者は 50 歳以前に死亡しており, 親に関しては死因および年齢から客観的な罹患有無の判断が可能であることがわかった.

孤発例の親は検討の結果, 59 名が非保因者と推定された. 親罹患家系と親非罹患家系との同胞の人数・年齢分布などの比較から, 同胞罹患者が親非罹患家系で低いのは真に親も同胞も非保因者であるためと考察された. 近親婚の調査より, 孤発例中劣性型が 17% 含まれている可能性が示唆された. 臨床データ分析より, 表型模写の存在が示唆された. 既知情報と考え合わせ, 本症の孤発例は不完全浸透 0%, 多発発現 16.1%, 未発症または未確認 31.5%, 新生突然変異 28.9%, 劣性型 17.0%, 表型模写 6.5% と推定された.

B11. DNA Repair in Systemic Lupus Erythematosus: Akihide OHTA, Fumitaka MORITO, Toshiro NAGAYOSHI, Yoichi SETOGUCHI, Masaya YAMAGUCHI (Dept. Intern. Med., Saga Med. Sch., Saga), Hideo HAMAGUCHI (Dept. Hum. Genet., Univ. Tsukuba, Ibaraki), Kenji KAJIYAMA and Tomohiro KUSABA (1st. Dept. Intern. Med., Kyushu Univ., Fukuoka)

In 1976 Beighlie and Teplitz have shown that lymphocytes from patients with systemic lupus erythematosus (SLE) have a defect in their DNA repair mechanism which is at least one of the etiologic factors. It is still unclear whether photosensitivity is significantly related to the pathogenesis of SLE, but we reported last year that fibroblasts from SLE

patients have approximately equal level of ultraviolet (UV)-damaged DNA repair to normal controls and in addition, serum from SLE patients has no effect on DNA repair. Thereafter, we have studied DNA repair of SLE cells in detail.

Materials and Methods: 1. Fibroblasts from skin of the SLE patients, normal controled patient with xeroderma pigmentosum (XP) and patient with Werner syndrome were studied, as to the following matter; 1) Unscheduled DNA synthesis (UDS) by autoradiography 2) survival rate and 3) growth rate after UV irradiation 4) UDS of each fibroblast colony. 2. UDS of lymphocytes from peripheral blood of SLE patients and normal controls were studied by scintillation counting.

Results and Discussion: There were no significant differences in UDS, survival rate and growth rate between fibroblasts from SLE patients and normal controls, though they were severely low in XP patient. In the colony studies, UDS of each colony was approximately in the same level but has some variation in either case of SLE patients and normal controls. Similarly UDS of peripheral lymphocytes from SLE patients and normal controls showed no significant difference. In summary, there were no significant differences in an ability to repair UV-induced damage of DNA between SLE patients and normal controls concerning at least fibroblasts and lymphocytes. Therefore we suggest that the mechanism of photosensitivity of the patients with SLE and the pathogenesis of SLE is not related to the defect of DNA repair.

**B12. ウィルムス腫瘍の遺伝: 松永 英 (国立遺伝研). Genetics of Wilms' Tumor:
Ei MATSUNAGA (Natl. Inst. Genet., Mishima)**

ウィルムス腫瘍と網膜芽細胞腫とは、その自然史において共通点が多い。しかしウィルムス腫瘍の遺伝については、まだ網膜芽細胞腫のように定説がなく、McKusickのカタログ (1978) を見ると「常染色体劣性 (未確定)」のカテゴリーに分類されている。

ウィルムス腫瘍が家系内の2人以上 (1卵性ふたごの一致例を除く) に出現している24家系を文献から集め、これについて分析した結果、その遺伝様式は常染色体劣性ではなく、不規則優性パターンに一致することがわかった。同一家系内に非発病・片側罹患・両側罹患の3型の保因者が出現しており、しかも患児のうちの両側例の割合および診断時年齢は、保因者親の表現度に応じて規則的に変動している。この所見は、演者が先に網膜芽細胞腫の遺伝に関して提唱した宿主抵抗性説とよく一致する。また、主遺伝子の伝達経路をたどると、細胞質遺伝を示唆する証拠は全くみられない。一方、全症例の99%は孤発例で、その約3%をしめる両側例はすべて遺伝性であるが、片側例の90%以上は非遺伝性とみなされる。要するにウィルムス腫瘍の遺伝は、網膜芽細胞腫のそれと本質的に同じと考えてよい。詳細は *Human Genet.* 57: 231-246, 1981 に発表。

- B13. 正常妊娠絨毛と完全奇胎絨毛における α -Fetoprotein の免疫組織化学的検索：**蔵重秀樹・小林邦彦・松尾清巧・梶井 正 (山口大・小児), 横田忠明・藤原茂芳 (山口大・一病理). **Localization of α -Fetoprotein in Chorionic Villi of Normal Placenta and Complete Hydatidiform Mole:** Hideki KURASHIGE, Kunihiko KOBAYASHI, Kiyosato MATSUO, Tadashi KAJII (Dept. Pediat., Yamaguchi Univ., Sch. Med., Ube), Tadaaki YOKOTA and Shigeyoshi FUJIHARA (1st. Dept. Pathol., Yamaguchi Univ., Sch. Med., Ube)

α -Fetoprotein (AFP) は、正常では胎児の肝臓、卵黄嚢で作られ、胎児や卵黄嚢の存在しない胞状奇胎では AFP は存在しないと考えられる。しかし、胞状奇胎で AFP が産生されたとする報告が散見されるため、胞状奇胎絨毛における AFP の存在の有無を Peroxidase-antiperoxidase 法を用いて免疫組織化学的に検索し、また、奇胎絨毛内液の AFP 濃度を Enzyme immunoassay 法を用いて測定した。

結果：正常妊娠絨毛 60 例中 13 例に AFP が陽性だった。陽性部位は、絨毛内の血管内血清、血管壁、血球であり、陽性例 13 例中 3 例は絨毛基質も陽性だった。妊娠週数と陽性率の間に特別な関係はなかった。完全奇胎は、30 例全例 AFP 陰性であった。したがって、正常絨毛群と胞状奇胎群には AFP 陽性率に有意差があった。(p<0.01 Fisher's test)。奇胎絨毛内 AFP 濃度は 17 例中 16 例が 20 ng/ml 以下で陰性と結論したが、1 例のみ 25 ng/ml を示した。

以上の結果から、奇胎絨毛に AFP が存在しないと結論することはできない。ただし、正常絨毛では AFP 陽性部が絨毛血管内に局在し、奇胎絨毛は血管を欠くか存在しても痕跡程度であることを考慮に入れると、奇胎絨毛には AFP が存在しないと考えた。

- B14. 完全奇胎トロホプラスト特異蛋白の検索：**萩原啓二・小林邦彦・梶井 正 (山口大・小児). **Studies on the Trophoblastic-Specific Proteins in Hydatidiform Mole:** Keiji HAGIWARA, Kunihiko KOBAYASHI and Tadashi KAJII (Dept. Pediat., Yamaguchi Univ., Sch. Med., Ube)

完全奇胎は雄核発生により生じ、父方遺伝子がホモ接合となっている“ヒト純系細胞”であり、正常トロホプラストとは異なる蛋白の存在の可能性がある。7.5% SDS-polyacrylamide 電気泳動では、奇胎絨毛内容液は母血清と類似パターンを呈した。血清蛋白 16 種の有無を免疫電気泳動で 8 例に行ったところ、albumin, α_1 -acid glycoprotein, α_1 -antitrypsin, Gc-globulin, α_1 -antichymotrypsin, ceruloplasmin, α_2 -HS glycoprotein, C₃, hemopexin, transferrin, IgA, IgG は全例陽性であり、prealbumin 7 例, haptoglobin 5 例, α_2 -macroglobulin 4 例それぞれ陽性であった。IgM は全例認めなかった。したがって、奇胎絨毛内容液は母血清を主成分とすると考えられた。正常絨毛では IgG のみが選択的に通過することからみて、奇胎トロホプラストでは母血清の選択性が欠如していると考えた。

なお、トロホプラスト特異蛋白の検出には内容液で家兎を免疫し、その血清を正常ヒト血清で吸収したものを用いて免疫電気泳動を行ったが、特異蛋白は同定できなかった。しかし、7.5% SDS-polyacrylamide 電気泳動法で、奇胎トロホプラスト抽出液に正常トロホプラスト微小絨毛抽出液に存在しない蛋白を認めた。分子量はそれぞれ、約 59,000, 58,000, 52,000, 35,000 であった。

B15. Esterase D Polymorphism in Hydatidiform Mole: Keiji HAGIWARA, Kunihiko KOBAYASHI and Tadashi KAJII (Dept. Pediat., Yamaguchi Univ., Sch. Med., Ube)

Classic hydatidiform mole is the product of an abnormal pregnancy with grossly swollen chorionic villi, without an embryo, cord or amniotic membrane. Histologically, the villi are characterized by advanced hyperplasia and anaplasia of the trophoblast, edema of the stroma and the absence of fetal capillaries. It is conceivable that the origin of the proteins in the molar stroma are the transduction of maternal serum, or the product of the trophoblast. Recently, the EsD polymorphism has been used for studying the origin of hydatidiform mole. We examined the EsD genotype of the molar trophoblast, stroma's fluid and both parents by starch-gel electrophoresis in 8 cases. The method used for EsD genotype was performed according to Hopkinson *et al.* (1968). The buffer system was Tris-borate-citrate-lithium hydroxide at pH 7.2. Electrophoresis was carried out overnight for about 21 hr at 4°C at 5 V/cm. In the preparation of the molar tissue, moles were collected as soon as possible after evacuation or hysterectomy. The whole specimen was washed in physiologic saline in order to eliminate the maternal blood and decidua. The individual mole vesicles were pierced with a needle and punctured by syringe. The fluid from the vesicles was centrifuged for 20 min 15,000 rpm after where supernatant was collected. The cellular debris was washed three times.

Electrophoretically, the relative intensity of the fluorescent band of EsD are as follows: parental red blood cell > trophoblast >> stroma's fluid. No abnormal bands were detected in molar tissue. The genotype of the trophoblast and stroma's fluid were same in all cases. No maternal genotype were detected in stroma's fluid. These data suggest that EsD's gene was expressed in molar trophoblast and the EsD in the stroma's fluid is originated from the trophoblast. Even if the transduction of maternal EsD is exist, the amount is very small and does not interface the genotyping. We think EsD is the suitable genetic marker for studying the origin of mole.

B16. Practical Application for Prenatal Diagnosis of Cell Growth Promoting Factor from Human Placenta: Tomoko HASHIMOTO, Shinobu GAMOU, Jun-ichi FURUYAMA (Dept. Genet., Hyogo Med. Coll., Nishinomiya), Kazuo NAKAMURA and Tsuneo TOMITA (Lab. Org. Chem., Mukogawa Women's Univ., Nishinomiya)

The rate of proliferation of human cells in culture is limited by the concentration of serum and other hormone-like agents. Recently, many papers were published on these factors. We also reported the new growth promoting factor obtained from human placental chorionic villi. This growth promoting factor was extracted according to the

method described by Gospodarowicz. This placental extract stimulated DNA, RNA, and protein synthesis and cell growth in human cultured fibroblasts when it was added to Eagle's minimum essential medium containing 0.4–10% fetal calf serum at a concentration of 100 $\mu\text{g/ml}$.

We demonstrated here that the placental extract had an ability to stimulate cell division of both cell line and primary cultured cells derived from amniotic fluid. When 100 $\mu\text{g/ml}$ of placental extract was added to the culture medium of cell line (F10+0.4–20% FCS), cell number per plate reached to twice of control at three day's incubation. When placental extract was supplemented to primary culture of amniotic fluid cells at a concentration of 100 $\mu\text{g/ml}$, the rate of cell number to control was 6.07 ± 5.71 (in 24 samples) and the rate of colony number was 1.75 ± 1.10 . These facts showed that placental extract could not increase the plating efficiency of primary cultured amniotic fluid cells but could induce cell proliferation. From chromosomal analysis study, there was no difference in chromosome number distribution and frequency of aberrations between culture conditions with or without placental extract.

Then the use of placental extract can minimize the time required between amniocentesis and diagnosis, especially when plenty of cells are required for diagnosis.

B17. $\gamma 3$ Gene Duplication in a Pair of Twins. Unequal Cross-Over or Chimerism?

Tokiko MIYAZAKI, Hideo MATSUMOTO (Dept. Leg. Med., Osaka Med. Sch., Takatsuki), **Hiroko FUJITA** (Dept. Child Health, Osaka City Univ., Osaka) and **Noboru ODA** (Dept. Psychiat., Osaka City Univ., Osaka)

A Japanese family with the dizygotic twins (male, aged 7), one of whom has three Gm haplotypes containing at least three $\gamma 3$ alleles, was encountered by a zygosity test. The 28 genetic marker systems have been investigated for the twins including the family members. The twins were diagnosed as dizygotic because of the differences in five systems; MNSs, Gc, AP, UMPK and HLA. Neither of the twins has ever had a blood transfusion. All the investigation on the twins was done on three different bleedings over a period of two years and no difference was found in the findings.

Concerning the Gm system, in the family there are the following $\gamma 1$ – $\gamma 3$ alleles: (1) z,a,x;g (2) z,a;b,b,s,t (3) f,a;b⁰,b¹,b²,b⁴,b⁵. The parents in the family each has only two $\gamma 1$ – $\gamma 3$ alleles: the father, (1) and (2); the mother, (2) and (3). One of the twins has inherited the $\gamma 1$ – $\gamma 3$ allele (1) from his father and the allele (3) from his mother. Another of the twins has inherited the allele (1) from his father, and the allele (3) from his mother, and the allele (2) either from his father or mother. Simultaneous presence of all the three alleles can only be explained by admitting chimerism or duplication by crossing-over. Neither the genetic marker systems on red and white blood cells, nor polymorphic auto-

somal markers detected by G-, C-, and Q-banding techniques demonstrated positively the existence of the chimerism in a pair of twins. The mechanism which resulted in the $\gamma 3$ duplication is postulated as being either unequal intercistronic or intragenic crossover. This seems to be the first such case to be found.

B18. Immunochemical Studies on Blood Group Active Glycoprotein and Glycolipid

Fractions from Human Red Cell Membrane: Ken FURUKAWA and Tadahisa

KOGURE (Dept. Legal Med., Gunma Univ. Sch. Med., Maebashi)

Lithium di-iodosalicylate (LIS) was used to extract glycoprotein fraction from erythrocyte stroma (Marchesi *et al.* 1972). Erythrocyte stroma was suspended in 0.3 M LIS and 0.05 M Tris-buffer, pH 7.5. After stirring for 15 min at 25°C, two volumes of water was added and the suspension was stirred for additional 10 min at 4°C. After centrifugation ($45,000 \times g$ for 90 min), the supernatant solution was mixed with an equal volume of 50% phenol in water with stirring for 15 min. To upper phase obtained by centrifugation at $4,000 \times g$, 4 volumes of ethanol was added. Precipitate obtained by centrifugation was dissolved in saline. Glycolipid fraction was extracted by the method of Hakomori *et al.* (1972). The red cell stroma was heated with ethanol in a water bath at 80°C and was kept at the boiling point for a 4 min. It was filtered and the filtrate was allowed to stand at -10°C for a few days. The precipitate was centrifuged and dried in a desiccator. The dry precipitate was washed with ether. The ether-insoluble precipitate was extracted with chloroform-methanol (1 : 2). The extract was suspended in saline by sonication.

The glycoprotein fraction isolated from red cell membrane by LIS, possessed serologically active specificities for ABH, MNSs and Duffy blood groups. The glycoprotein fraction showed strong inhibitory capacity against human and chicken anti-H, and moderate activity against *Ulex* I and *Ulex* II lectins. Weakly inhibitory activity of the glycoprotein against eel anti-H indicated that immunochemical structures of H active red cell glycoprotein may similar to that the salivary and the duodenal water-soluble H substances.

The glycolipid fraction obtained from red cell membrane by ethanol and chloroform-methanol mixture, possessed specific activities for ABH, Lewis, P and I blood groups as already reported. Weak anti-Rh₀(D) inhibiting activity was demonstrated in the glycolipid fraction.

Inhibiting activity of glycoprotein fraction against *Ricinus communis* lectin which directed to β -galactosyl residues was much stronger than that of glycolipid fraction. The agglutination of *Psathyrella velutina* lectin with human red cells which directed to *N*-acetylglucosaminyl residues was inhibited both strongly with the glycoprotein and glycolipid fractions. Action of β -galactosidase from *Clostridium tertium* on the glycoprotein fraction destroyed

the inhibiting capacity against *R. communis* lectin, and increased in activity of the enzyme-treated glycoprotein against *P. velutina* lectin was observed. Neuraminidase from *Vibrio cholerae* destroyed MNSs activities in glycoprotein fraction with a development of T specificity, and the β -galactosidase from *Cl. tertium* did not decreased the T activity of neuraminidase-treated glycoprotein.

It was observed that Kell, Lutheran, Kidd and Xg activities were neither present in the glycoprotein nor the glycolipid fractions. The findings therefore indicate that the immunochemical characteristics of these antigens may dissimilar to that ABH, Lewis, P, MNSs, I, Rh and Duffy red cell antigens.

B19. The Rare Kell Blood Phenotype $K_p(a-b-c+)$ with a Possible Genotype K_p^e/K^o in a Japanese Family (a second report): Yasuto OKUBO, Taiko SENO, Hideo YAMAGUCHI, Masayoshi TANAKA (Osaka Red Cross Blood Cent., Osaka) and Masaki KIKUCHI (Miyagi Red Cross Blood Cent., Sendai)

In 1979 a new phenotype of the Kell system $K_p(a-b-c+)$ due to a third allele of the K_p locus was first recognized by us. Since then another four examples of this rare phenotype have been detected in Japan. This report describes a sixth such rare phenotype detected in the Miyagi Red Cross Blood Center.

The propositus is a 22-year-old female healthy donor whose blood was brought to our attention in the antigen screening tests of 30,133 Miyagi donors as a negative example with anti- K_p^b . She was found to be $K_p(a-b-c+)$.

The family study revealed that the proposita's mother was not $K_p(a-b+c+)$ but $K_p(a-b+c-)$, though her father was $K_p(a-b+c+)$ as was expected. Accordingly the proposita's possible genotype was assumed to be not K_p^e/K_p^e but K_p^e/K^o .

In Miyagi donors the roughly estimated gene frequency of K^o was 0.0054 and that of K_p^e 0.00093. Consequently, the expected frequency of the heterozygote K_p^e/K^o was estimated to be 0.000106 (1 in 94,339).

Acknowledgement: We wish to thank Dr. G.L. Daniels, MRC London, for his co-operation in this study.

B20. An Unusual Case of Blood Group ABO Inheritance. O From $AB \times O$: Yogo OKA, Norio NIKAWA (Dept. Pediat., Hokkaido Univ. Sch. Med., Sapporo), Akira YOSHIDA (Dept. Biochem. Genet., City Hope Res. Inst., Duarte, U.S.A.) and Hideo MATSUMOTO (Dept. Forens. Med., Osaka Med. Coll., Takatsuki)

An unusual blood group inheritance, *i.e.* a phenotype O child from an $AB \times O$ parents, was found in a Japanese family. Since two other children from the parents are blood type B, this is not a case of Cis-AB inheritance. The mother is not blood A/B chimera,

and normal levels of blood group *N*-acetylgalactosaminyltransferase (A-enzyme) and galactosyltransferase (B-enzyme) were detected in her plasma. Therefore, the mother is genetically true *AB* heterozygous. The two sons with phenotype B had normal levels of plasma B-enzyme, but had no A-enzyme, and the father and the daughter with phenotype O had neither A- nor B-enzyme in their plasma. The analyses of 24 genetic marker systems indicated that the O daughter was a true child of the parents.

The affirmative probability of parentage on the O daughter was calculated to be 0.9999999917 by Bayes' theorem.

We concluded that the genotype of the O daughter was not the usual *OO*, and that this rare O expression might be due to a new structural mutation or a deletion in either maternal A or B gene, during oogenesis.

B21. Genetic Polymorphism of the Human Coagulation Factor XIII (A subunit and B subunit) in Japanese: Toshinori NISHIGAKI, Keichi OMOTO (Dept. Anthropol., Univ. Tokyo, Tokyo), Makoto UCHIKAWA (Blood Transfus. Serv., Tokyo Univ. Hosp., Tokyo) and Takeo JUJI (Blood Transfus. Serv., Tokyo Women's Med. Coll., Tokyo)

In plasma, human coagulation factor XIII is comprised of two A subunits and two B subunits (A_2B_2). Genetic polymorphisms of the A subunit and the B subunit were first described by Board (1979, 1980) in Australian Caucasians. In the present study, polymorphisms of both subunits in Japanese were investigated.

Polymorphism of the A subunit was investigated in a total of 595 plasma samples from unrelated Japanese using an agarose gel electrophoresis followed by a fluorescent technique for the localization of transglutaminase activity. Three common phenotypes, 1, 2-1 and 2, were observed. The family material from 23 matings with 60 children indicated that these phenotypes are controlled by a pair of autosomal, codominant alleles. The estimated allele frequencies of *F13A*1* and *F13A*2* were 0.886 and 0.114, respectively.

Polymorphism of the B subunit was also investigated in a total of 119 plasma samples using an agarose gel electrophoresis followed by immunofixation. Three common phenotypes were observed, which corresponded to the phenotypes 1, 3-1 and 3 reported by Board (1980). The other types (2-1 and 3-2) reported by Board were not observed in the present study. The observed numbers of the phenotypes were in good agreement with those expected on the basis of Hardy-Weinberg's law. The allele frequencies of *F13B*1* and *F13B*3* were estimated at 0.303 and 0.697, respectively.

**B22. Polymorphism of Aldehyde Dehydrogenase and Abnormal Aldehyde Metabolism
in Japanese: Shoji HARADA (Inst. Community Med., Univ. Tsukuba, Ibaraki)**

In our previous studies, we presented that aldehyde dehydrogenase (ALDH) in Japanese showed polymorphism and individuals possessing the only high K_m enzyme would be exposed to an elevated acetaldehyde (ACT) concentration in blood after alcohol intake. However, no studies regarding the association between the phenotypes of ALDH and blood ACT concentration after alcohol intake have been so far reported.

In the present studies, the phenotypes of ALDH-I (normal and deficient types of low K_m enzyme) in hair roots were determined concerning 40 healthy Japanese using polyacrylamide gel isoelectric focusing, and the blood ACT concentration after oral dose of alcohol (0.5 g/kg body weight) were also determined on the same individuals using gas chromatograph with FID detector (Perkin-Elmer). Chromosorb 101 was used as the carrier medium in a $3 \times 1,500$ mm column.

A total of 43% of Japanese who are deficient in the ALDH-I isozyme showed flushing symptom and higher concentration of blood ACT ($37.3 \mu\text{M}$) than that of subjects with normal type of ALDH-I ($2.1 \mu\text{M}$).

Our data support that deficient type of ALDH-I is mainly responsible for the raised blood ACT levels associated with flushing symptom in Mongoloid population. Individuals deficient in the low K_m enzyme of ALDH would be exposed in higher level of ACT and may be at higher risk of acetaldehyde-related organ damage due to alcohol abuse.

**B23. Genetic Activity Variants of Erythrocyte Glucose Phosphate Isomerase (GPI):
Chiyoko SATOH, Akiko YAMASHITA, Chiemi KAWAMOTO, Hiroko ARA-
KAWA, Hideo OMINE, Mikio FUJITA and Kazuaki GORIKI (RERF, Hiro-
shima)**

In an attempt to detect variant proteins not detectable by electrophoresis, screening is done using enzyme activity as a marker. This report presents the results obtained for glucose phosphate isomerase (GPI). After drawing blood using ACD as anticoagulant, red blood cells were separated and washed, and 1/20 hemolysate was prepared using β -mercaptoethanol-EDTA. Using $5 \mu\text{l}$ of this hemolysate GPI activity was determined by a Roto Chem IIa (Aminco Co.) according to the ICSH method (1977). Using half of the hemolysate, electrophoretic phenotyping was made by starch gel electrophoresis using Tris-citrate buffer, pH 8 of Detter *et al.* Examination of 1,231 children of proximally and distally exposed A-bomb survivors in Hiroshima demonstrated that the electrophoretic phenotype of 1,226 children was GPI 1, mean activity 34.8 IU/g Hb , S.D. 3.3 IU/g Hb .

For 4 children whose electrophoretic phenotype was GPI 1, the enzyme activities were found to be lower than 66% of the normal value (49%, 56%, 56% and 63%). The pheno-

types of all their parents were GPI 1, the activity of one of the parents in three cases, being less than 66% of the normal value, while that of the other was normal in these three cases. The K_m F6P and the thermostability of the GPI with decreased activity in these three cases were normal. In the fourth case, however, K_m F6P was normal for both parents and the propositus, but the remaining activities of GPI in the hemolysates of the propositus and her mother after heating for 50 min at 50°C in 20 mM triethanolamine buffer, pH 8.2, were 53% and 56%, respectively, of normal GPI 1.

These findings suggest the presence of a thermo-labile allele in the fourth case and the possibility of a null allele *GPI*⁰ in the first three cases.

B24. Population Analysis of Associations among C2, BF, and HLAA, B, C Markers in Japanese: Katsushi TOKUNAGA, Keiichi OMOTO (Dept. Anthropol., Univ. Tokyo, Tokyo), Chieko ARAKI (Dept. Res., Red Cross Cent. Blood Cent., Tokyo) and Takeo JUJI (Blood Transfus. Serv., Tokyo Women's Med. Coll., Tokyo)

Association between the alleles of C2, BF, and HLAA, B, C was analysed in a Japanese population material. Blood samples obtained from about 500 unrelated healthy adult Japanese living in Tokyo were typed for C2, BF, and HLAA, B, C. The following two-factor combinations were suggested to be in positive linkage disequilibrium: C2*AT-A*26, C2*AT-B*15, C2*B-B*w61, BF*F-A*w33, BF*S-A*11, BF*S-A*w24, BF*F-B*15, BF*F-B*17, BF*F-B*w44, BF*S-B*7, BF*S-B*w52, BF*S-B*w54, BF*S-B*w59, BF*F-C*w3, C2*AT-BF*F, and C2*A'-BF*F. Taking the association data on HLAA, B, C into consideration, the following haplotypes are considered to be characteristic in Japanese: C2*AT-BF*F-B*15-C*w3-A*26, BF*F-B*w44-A*w33, BF*S-B*7-A*w24, BF*S-B*w52-A*w24, BF*S-B*w54-A*11, and BF*F-B*17-C*w3. Most of these combinations were different from those reported in Caucasians.

We consider that not all of these associations have been maintained by selective pressure, but most occurred relatively recently in human evolution mainly by admixture among subpopulations or by random genetic drift.

B25. らいの免疫遺伝学: 菊池郁夫・笹月健彦 (東医歯大・人類遺伝), 小沢利治 (国立多摩研), 左奈田精孝・小関正倫 (多摩全生園). Immunogenetics of Leprosy: Ikuo KIKUCHI, Takehiko Sasazuki (Dept. Hum. Genet., Tokyo Med. Dent. Univ., Tokyo), Toshiharu OZAWA (Natl. Inst. for Leprosy Res., Higashimurayama), Kiyotaka SANADA and Masanori KOSEKI (Natl. Sanat. Tama-Zenshoen., Higashimurayama)

T,BT 型患者 20 名, L 型患者 32 名の *in vitro* 二次免疫応答を, ³H-チミジン芽球内取り込みによって検討した. PPD 抗原, 溶連菌細胞壁抗原に対しては L 型, T,BT 型ともに反応に差は認められ

なかったが、らい菌抗原に対して、T,BT 型はよく反応したが、L 型は全く反応せず、この非応答性はらい菌抗原の量を変えても変化がなかった。このことから L 型患者はらい菌抗原に反応しなく、かつその非応答性が抗原特異的であることが示された。次に、T 型患者、L 型患者の T 細胞、モノサイトの間の相互作用を検索したところ、L 型患者のモノサイトは T 型患者の T 細胞と組み合わせると反応するが、L 型の T 細胞を T 型のモノサイトと組み合わせても反応はおこらず、このことから L 型の抗原特異的免疫非応答性が T 細胞レベルで規定されていることが明らかにされた。HLA 抗原系の検索によって、T 型患者と HLA-DR2, MT-1 との相関が観察された。

B26. Immunogenetic Analysis of Post Schistosomal Liver Cirrhosis in Man: Nobuo OHTA, Takehiko SASAZUKI (Dept. Hum. Genet., Tokyo Med. Dent. Univ., Tokyo) and Masahiko IUCHI (Dept. Int. Med., Kofu City Hosp., Kofu)

Immunogenetic factors involved in pathogenesis of post schistosomal liver cirrhosis in man were investigated. One hundred and twenty one patients with post schistosomal liver cirrhosis served as subjects. Almost all patients (93.6%) showed strong immune response to schistosomal adult worm antigen. In the random population infected with *Schistosoma japonicum* 10 out of 57 (17.5%) were low responders. There were thus significant fewer low responders to schistosomal adult worm antigen in the patients than in the infected controls ($p < 0.05$). We also observed significant decrease in frequency of HLA-Bw52-Dw12 haplotype in the patients ($H_f = 0.013$) compared to normal controls ($H_f = 0.097$) ($p < 0.01$). We already observed that an immune suppression gene for schistosomal adult worm antigen might be in strong linkage disequilibrium with HLA-Bw52-Dw12 haplotype in the random population. The significant decrease of HLA-Bw52-Dw12 haplotype in the patient group suggested the absence of immune suppression gene in the patients, and this was consistent with the fact that almost all patients showed strong response to schistosomal adult worm antigen. These observation strongly suggested that an HLA-linked immune suppression gene, which is in strong linkage disequilibrium with HLA-Bw52-Dw12 haplotype, controls the immune responsiveness to schistosomal antigen and susceptibility or resistance to liver cirrhosis in schistosomiasis japonica in man.

B27. An HLA Linked Immune Suppression Gene to Streptococcal Cell Wall Antigen in Man: Yasuharu NISHIMURA, Toshio SONE and Takehiko SASAZUKI (Dept. Hum. Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

Genetic control of the immune responsiveness to streptococcal cell wall (SCW) antigen in man was analyzed using eleven pairs of monozygotic twin, 130 members of 18 families and 149 unrelated healthy adults. Secondly immune response of peripheral blood lymphocytes (PBL) was examined by antigen specific T cell proliferation *in vitro*.

Correlation of the immune responsiveness to SCW antigen was very high ($r = 0.787$) between monozygotic twins. Distribution of the immune responsiveness could be divided

into high and low responsiveness among family members, and family analysis by maximum likelihood scoring method revealed that the low responsiveness to SCW antigen was controlled by single dominant gene.

Correlation of the immune responsiveness to SCW antigen was very high ($r=0.911$) between HLA-identical siblings, and was relatively low ($r=0.460$) between HLA-haplo-identical siblings and was negative ($r=-0.282$) between HLA-nonidentical siblings. This single dominant gene which control the low responsiveness to SCW antigen was shown to be closely linked to HLA (lod score was 3.709 at $\theta=0.00$) by the Morton's sequential linkage test. Furthermore, this gene was in positive linkage disequilibrium with HLA-Aw24 and HLA-DR supertypic MT1 and was in negative linkage disequilibrium with HLA-DR4 and HLA-DR supertypic MT3. Gene frequency of this gene was calculated as 0.462 by checking the immune responsiveness of 149 unrelated healthy adults.

T cells from one of the low responders could suppress the proliferative immune response of PBL to SCW antigen in high responder, who was HLA-DR identical with low responder. Low responsiveness to SCW antigen was, therefore, controlled by suppressor T cells and an HLA-linked dominant gene for low responsiveness to SCW antigen should be immune suppression gene to SCW antigen (Is-SCW).

B28. Immunogenetic Analysis of Autoimmune Thyroiditis III: Hisamitsu UNO, Takehiko SASAZUKI (Dept. Hum. Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo), **Hajime TAMAI** (Dept. Psychosom. Med, Kyushu Univ., Fukuoka), **Junji KONISHI** (Dept. Nucl. Med., Kyoto Univ., Kyoto) and **Hideo MATSUMOTO** (Dept. Legal Med., Osaka Med. Coll., Takatsuki)

Previously we showed evidence for existence of two major genes controlling susceptibility to Graves' disease (GD): one is closely linked to HLA-DR, the other linked to gene coding for Gm allotype.

The mode of inheritance and gene frequencies of these two genes were inferred by affected sibpair method. Out of 15 affected sibpairs 8 shared two HLA haplotypes and 7 shared one HLA haplotype. This haplotype distribution showed the minimum chi-square for an HLA-linked recessive gene with gene frequency 0.30. Gene frequency 0.08 was also obtained under the dominant model at this chi-square. The mode of inheritance and gene frequency of a Gm-linked gene were estimated by the observed incidence of GD in Japanese population (8/10,000) supposed high penetrance of GD. Under both recessive and dominant model for an HLA-linked gene, a Gm-linked gene was inferred to be a recessive gene frequency 0.10.

Secondly, the immunogenetic factors of Hashimoto's thyroiditis (HT) were investigated using two groups of multiple case families. Analysis of 7 families affected with both GD

and HT indicated that common HLA-linked disease-susceptibility gene contributed to the onset of GD and HT. Eleven families, where family members were affected with HT, were also typed for HLA and Gm. The mode of an HLA-linked disease susceptibility gene to GD and HT was, then, inferred from the distribution of HLA haplotype in 33 affected sibpairs of either GD or HT. Consequently, an HLA-linked gene was estimated to be either dominant with gene frequency 0.08 or recessive with gene frequency 0.47. In both cases, the second locus linked to Gm loci was expected because of the low penetrance of GD and HT under that gene frequencies.

B29. Immunogenetic Analysis of Cryptomeria Pollinosis: Masahiko MUTOH, Takehiko SASAZUKI (Dept. Hum. Genet., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo) **and Yozo SAITO** (Dept. Otolaryngol., Tokyo Med. Dent. Univ., Tokyo)

Ninety-five probands involving 621 family members and 17 affected sibpairs with Cryptomeria Pollinosis (CP) were investigated with respect to immunogenetic factors for the development of CP. Complete correlation was demonstrated between CP and immune responsiveness (IgE) to cryptomeria pollen antigen, because the patients with CP produce IgE antibody to cryptomeria pollen antigen whereas the healthy family members did not respond to the antigen. Affected sibpair method revealed an HLA-linked disease susceptibility locus for CP. This method could not distinguish the recessive model ($gf=0.38$) and dominant model ($gf=0.07$) for the HLA-linked disease susceptibility locus. Therefore, Immune responsiveness (IgE) to cryptomeria pollen antigen was controlled by an HLA-linked gene. Additionally, proband method indicated that CP might be controlled by a single recessive gene (penetrance >0.6). Namely, the HLA-linked gene controlling the low responsiveness (IgE) to cryptomeria pollen antigen was dominant (an HLA-linked immune suppression gene). And the HLA-linked immune suppression gene controls the resistance to cryptomeria pollen antigen.

B30. The Immunological Functions of the Children with Down Syndrome: Atsumi KOMURO, Munehiro HIRAYAMA (Dept. Matern. Child Health, Univ. Tokyo Tokyo), **Masanori HAYAMI** (Dept. Measles Virus, NIH, Tokyo) **and Makoto HIGURASHI** (Dept. Public Health, Yamanashi Med. Sch., Kofu)

The children with Down syndrome have been suspected of having some kinds of immunological deficiency. In this study, several kinds of immunological functions of the children with Down syndrome were compared with those of normal controls, with which the speculation was made on the immunological deficiency that might exist in the children with Down syndrome.

Using the sera and leukocytes of peripheral blood from 14 donors of Down syndrome

(their average age was 2 years and 5 months old) and 7 of normals (their average age was 1 year and 7 months old), following items were investigated; serum immunoglobulin level, numbers of total and differential counts of leukocytes, T-cell and non-T-cell ratio of lymphocytes, blastogenic response of lymphocytes to PHA measured by thymidine uptake and IFN production, and the sensitivity of lymphocytes to IFN assayed by suppression of PHA response.

The children with Down syndrome showed significant decrease in the level of IgM, numbers of leukocytes and lymphocytes, and lymphocyte reactivity against PHA compared with normal children. On the contrary, blastogenesis of lymphocytes of the children with Down syndrome was suppressed by IFN more markedly than that of normal children, which suggested the hyper sensitivity of lymphocytes of the children with Down syndrome to IFN.

Taking these results into consideration, in the children with Down syndrome, the immunological functions were considered to be reduced in both quantity and quality.

- B31. 羊水の染色体分析結果について：林 美貴子・本田幸子・植竹久雄（富山県衛生研），渡辺正男・松田健史（富山医薬大）. Chromosome Analysis of Amniotic Fluid Cells: Mikiko HAYASHI, Sachiko HONDA, Hisao UETAKE (Toyama Inst. Health, Toyama), Masao WATANABE and Takeshi MATSUDA (Toyama Med. Pharm. Univ., Toyama)**

富山県衛生研究所における約 5 年間の羊水の染色体検査の結果，培養例数 66 例で，判定例数 57 例，うち 7 例が染色体異常であった。

以前トリソミー型ダウン症出産経験者 26 例のうち 3 例（症例 1, 2, 3）にトリソミー型の反復妊娠がみられ（11.5%），母が転座型あるいは逆位保因者である 4 例のうち，3 例（症例 4, 5, 6）が母と同じ保因者であった。また，母の高年齢妊娠 5 例のうち 1 例（症例 7）に 46,XY/46,XX のモザイクがみられた。一般にトリソミー型ダウン症の再発危険率は一般集団におけるダウン症の発生率よりも高いといわれるが（藤田，1977；鈴木，1981），当所での結果も検体数は少ないが同様の傾向を示した。うち，1 例は 3 回の G トリソミー反復妊娠例で，1 例は母親高年齢妊娠であった。症例 1；第 1 子 47,XY,+G 羊水 47,XX,+G。症例 2；第 1,2 子ともに 47,XX,+G 羊水 47,XX,+G。症例 3；第 1 子 47,XX,+G 羊水 47,XY,+E。症例 4；母 45,XX,t(14:21)，第 2 子 46,XX,-14,+t(14:21) 羊水 45,XY,t(14:21)。症例 5；母 46,XX,inv(3)，第 1 子 46,XX,rec(3) 羊水 46,XX,inv(3)。症例 6；母 45,XX,t(13:15) 羊水 45,XX,t(13:15)。症例 7；母 38 歳初妊娠，羊水 46,XY/46,XX。

B32. Parental Age Effects in Turner Syndrome: Hiroko FUJITA, Noriko MATSUMOTO, Yoko YOSHIDA, (Dept. Child Health, Osaka City Univ., Osaka) and Yoko TANIGAWA (Lab. Chromosome, Hyogo Prefect. Tsukaguchi Hosp., Hyogo)

Data on parental age in this investigation of 143 cases are based on both published and unpublished series of patients with Turner syndrome. One published study is of 28 cases out of 45 examined in Tottori University (Santo, 1975) during the period of 1958–74. Unpublished series are of 78 patients examined at special clinic for chromosome of Tsukaguchi Prefectural Hospital during of 1971–80 and the remaining were provided by some cooperating pediatricians. Available 505 chromosomally normal persons who visited the clinic in Tsukaguchi Hospital during the same period of 1971–80 were used as control, as there are only suitable vital statistics data for control of maternal age distribution at birth but no data for that of parental age. Five-year maternal age group distributions show no significant difference by birth year between the controls and annual vital statistics data for all live births in Japan.

Mean paternal ages on 45,X, 45,X/46,XX or 47,XXX, 46,Xi(Xq), 45,X/46,Xi(Xq) and partial monosomy of X chromosome were 31.6 ± 4.9 , 32.7 ± 3.7 , 32.7 ± 5.7 , 33.3 ± 5.1 and 29.6 ± 3.7 , respectively. These findings except for the partial deletion of X are higher than that of the control which is calculated as 30.6 ± 5.1 . Especially, there was a significant difference in 45,X/46,Xi(Xq) ($p < 0.01$).

The paternal age distributions of 5 year interval for 46,Xi(Xq) and 45,X/46,Xi(Xq) were significantly different from that of the control ($p < 0.05$).

Regarding to mean maternal ages and maternal age distributions in the all karyotype groups there were no significant difference from the control at all. As to pattern of relative incidence, the rising pattern with advancing paternal age appears not only in the group of iso-X chromosome but also in the 45,X including of its mosaics. On the other hand, the rising pattern with maternal age did not appear in the both karyotypes with exception for a slightly increase in 30–34 year-old mother group of 46,Xi(Xq).

B33. A Cytogenetic Study of 5,400 Newborn Infants: Yoshikazu KUROKI, Ichiro MATSUI (Kanagawa Child. Med. Cent., Yokohama), Nagakazu TSUNEKI and Itsuro OHSAKI (Kanagawa Matern. Child. Cent., Yokohama)

Data from a chromosome survey of 5,400 consecutive newborn infants is presented. Successful karyotypes were obtained on 5,026 babies (2,448 females and 2,578 males) using two day blood culture and conventional staining methods. Of those, 4,995 newborns had normal karyotypes, but 31 (0.62%) had a major chromosome abnormality. Six male babies with sex chromosome abnormalities were three 47,XXY and three 47,XYY

infants. Eight female infants showed one 45,X, four 45,X/46,XX, and three 47,XXX karyotypes. Four babies had 21 trisomy, one had 18 trisomy. Seven infants had a balanced chromosome rearrangement. Four of them were Robertsonian translocation and two were reciprocal type. One baby had an inversion. Six infants had an unbalanced structural rearrangement. Two were G/G translocation Down syndromes, one was 46,XY,Bq- and the other one infant had 46,XX,18p-. Remaining two cases showed a minute extra marker chromosome. In comparison with seven other similar studies, the incidence of Turner syndrome was high (0.2%) and that of Down syndrome was slightly reduced (0.8%).

B34. 認知された初期妊娠集団における染色体異常有病率の推定：山本正治・伊藤 隆・渡辺蔵一（新潟大・医・衛生）. Estimated Frequencies of Chromosome Anomalies Prior to the Clinical Manifestation of Spontaneous Abortions: Masaharu YAMAMOTO, Takashi ITO and Gen-ichi WATANABE (Dept. Hyg. Prev. Med., Niigata Univ., Niigata)

過去5カ年にわたる中絶症例の染色体異常の疫学研究から、妊娠3カ月までの異常頻度は6.5%であり、出生児集団の頻度に比べ約10倍高いことが判明した。

いま、認知された妊娠の約15%が流産に終わると仮定して自然流産および新生児集団の異常頻度から、認知された全妊娠集団での染色体異常有病率を推定したところ、全異常では6.8%の値を得た。観察値6.5%は、この値に近似しており、かつ核型別異常についても、その分布はほぼ類似していた。このことは、妊娠3カ月までの中絶症例の染色体分析が認知された妊娠中の異常発生状況を知る手がかりとなると考えられる。

しかし、今回の中絶例の母年齢分布は、日本の出産時母年齢分布に比べ35歳以上の分布割合が多いため、より正確な推定には母年齢を考慮する必要がある。われわれは、中絶集団における核型別異常頻度を1975年の一般出産集団の年齢分布で重みづけを行うことによって、一般集団における認知された妊娠中の染色体異常有病率を推定した。

トリソミー型異常では30%、モノソミー型異常では0.6%、3倍体では0.7%、4倍体では0.5%、構造異常では0.1%、全異常では5.0%となった。今回の分析における出産集団は、自然流産による淘汰選別をうけた集団であり、流産発生前の年齢分布は出産集団の年齢分布と異なる可能性がある。そこで、この点についても考慮した分析が今後必要であると考えられる。

B35. 奇形に関する遺伝相談の追跡調査：佐藤孝道・加藤康子・香山文美・鈴木 明・堤 治・森田良子・神保利春・水野正彦・坂元正一（東大・医・産婦）. A Follow-up Study of Genetic Counselling for Malformations: K. SATO, Y. KATO, F. KAYAMA, A. SUZUKI, O. TSUTSUMI, Y. MORITA, T. JIMBO, M. MIZUNO and S. SAKAMOTO (Dept. Obst. Gynecol., Univ. Tokyo, Tokyo)

奇形は、その種類が複雑多岐にわたり、また遺伝的異質性の存在によって、危険率を推定するうえで困難を感じることが多い。一方、実際に遺伝相談を行った後の妊娠・分娩に関する prospective な調査報告もほとんどない。そこで、今回、1976年から1980年の5年間に奇形児分娩の既往を主訴と

して当科遺伝外来を訪れた 71 例を対象とし、推定した危険率とその後出産した児の奇形発生頻度との関係を検討した。71 例中、19 例が計 22 回の分娩をしたことが追跡調査の結果明らかとなった。このうち 14 例 17 分娩は危険率が 1.0% 未満と推定したが、その 1 例 (5.9%) に anencephalus が、また 5 例 5 分娩は危険率が 10% 以上と推定したが、その 2 例 (40.0%) に、hydrocephalus と Meckel syndrome の児が出産している。奇形があった 3 例とも、胎児診断によって出生前に診断を確定した。

以上の調査によって、困難な点の多い奇形に関する遺伝相談も、診断の確定、正確な家系図の作成、遺伝的異質性の考慮等によって、危険率の推定がほぼ満足すべき正確さで行なわれうることが明らかとなった。

B36. Follow-up Study of Genetic Counseling (X): Norio FUJIKI, Kazuo MANO
(Dept. Int. Med., Fukui Med. Sch., Fukui), Itsuro NISHIGAKI and Yasuko SHIRAI (Inst. Dev. Res., Kasugai)

We have experienced 2,003 cases of genetic counseling at five different counseling centers since 1961. The contents consist of 693 cases (22.7%) of hereditary disease including metabolic anomaly, 532 cases (17.4%) of constitutional disease like schizophrenia and diabetes, 485 cases (15.8%) of nongenetic factors such as irradiation, medication or infection during pregnancy, 468 cases (15.3%) of consanguinity, 464 cases (15.2%) of malformation like harelip and cleft palate, 152 cases (5.0%) of blood incompatibility, 84 cases (2.7%) of chromosomal anomaly, and 182 cases (5.9%) of others. Accumulatively 3,060 cases were counted, which meant one third of cases had plural problems.

As follow-up study, we analyzed 201 counselees who answered questionnaire as soon as they had decided their mind after counseling. Twelve cases regarded their situation as high risk before counseling, and 24 cases resulted in breaking engagement, avoiding pregnancy or performing arteficial abortion after counseling.

We performed comparative study on genetics among internists, medical students, and public health nurses as well as counselees. Even medical students misunderstood congenital anomalies were rare and would be shocked if they were informed carrier of some hereditary disease. Enlightenment is by all means necessary for the public.

B37. 当教室における先天奇形 102 例の臨床的検討：竹内 泉・片桐清一・斉藤 勝
(弘前大・産婦). **Clinical Statistics of Congenital Anomalies—102 Cases in the Department of Obstetrics, Hirosaki University: Izumi TAKEUCHI, Seich KATAGIRI and Masaru SAITO** (Dept. Obst. Gynec., Hirosaki Univ., Sch. Med., Hirosaki)

周産期医療の発達とともに周産期死亡は減少してきているが、それとともに先天異常の周産期死亡に占める割合が大きくなっていると思われる。そこで、弘前大学附属病院産科における昭和 41 年から昭和 55 年までの過去 15 年間にみられた外表奇形について検索した。

奇形児総数は 102 例で、その頻度は 1.6% であった。周産期に死亡した奇形児は 19 例あり、その

周産期死亡に占る割合は15.9%であった。奇形児出産数は漸増傾向にあり、とくに周産期死亡に占める割合は増加傾向にあった。母親が高年齢になるとともにその頻度は高くなる傾向を示し、とくに35歳以上に頻度が増加していた。奇形の種類では、口唇・口蓋裂が最も多く、ついで内反足、無脳児・半脳児がこれに続いていた。周産期死亡をきたした奇形としては、無脳児・半脳児が最も多く、ついで腹壁破裂であった。

遺伝因子の関与を検討したが、右多趾症を反復した例があった以外に、家族歴、既往分娩歴に異常のみられた例はなかった。環境汚染などに伴い、先天奇形児の出産頻度は増加しつつあると考えられ、先天異常児出生予防に対するよりいっそうの対策が重要であると思われる。

B38. 先天性心疾患の遺伝要因の検討：木下良順・井上徳治（久留米大・医・法医），大石喜六・古賀道弘（久留米大・医・二外）. Genetical Study of Congenital Heart Diseases: Yoshinori KINOSHITA, Tokuji INOUE (Dept. Legal Med., Kurume Univ., Sch. Med., Kurume), Kiroku OHISHI and Michihiro KOGA (Dept. 2nd Surg., Kurume Univ., Sch. Med., Kurume)

先天性心疾患（以下、CHD）に対する診断、外科的手技の進歩によって、救命される症例が増加し、それに伴いCHDの遺伝や成因についての関心が高まってきた。

そこで、私どもは、久留米大学病院第二外科で、手術によって心内奇形が確認され、かつ成因不明なCHD 1,436例について、遺伝および環境要因の検討を行い、次の成績を得た。

I) 遺伝要因

1) 家族集積性がみられ、発端者の第1度近親に最も多く再発生が認められた。2) 同胞における再発生実測値は1.52%で、一般人口の発生頻度の約2倍を示し、また、子における再発生実測値は4.97%で、約7倍を示した。3) CHDの遺伝様式は、heritability 40~60%の多因子遺伝であることがNewcombeのグラフで示唆された。4) 双生児において、ともにCHDであったのはすべて一卵性双生児で、その一致率は25%であった。5) CHDとHLAおよびGm型との間に、とくに相関関係は認めなかった。

II) 環境要因

1) 分娩時年齢が35歳以上になると、相対性危険率が上昇する傾向が認められた。2) 出生順位では、心室中隔欠損症の場合に、第2子に多く認められた。

B39. Frequency of the Genetic Disease within Patients of the Head and/or Limb Lesion by Group Congenital Malformation Examinations: Mitsushiro KIDA, Mariko UEHARA and Kooichi YOSHIMURA (Dept. Pediat., Teikyo Univ. Sch. Med., Tokyo)

It is no wonder that the surveillance system of congenital malformation should be regarded as important and are possessed of many subjects should be solved. In one of those subjects there are selection of the harmful factor to human beings before their birth period in living environment. At many diseases, that are caused by harmful factor before birth, namely mutagen and teratogen, embryopathy and fetopathy (teratogen) influenced during a time limit to one generation, however genetic disease (mutagen) continue during many

generations practically, that is to say it effects over the future of mankind. The other hand, many symptoms at the parts of the head and limb are able to found and used to diagnose, so it was considered that the frequency of the genetic diseases in those groups are important for the estimation of environmental harmful factor especially genetic factor or mutagens.

The object of this study are 288 patients, who took medical advice by group examination within a period from March 1980 to October 1981 at 10 area 11 place, at Hiroshima 18 patients, Toyama 5, Fukuoka 24, Teikyo Univ. 15, Tokyo 32, Saitama 43, Yamagata 21, Shizuoka 17, Takamatsu 23, Chiba 51, and Nagano 39. In 288, 27 patients had no symptom of limb or head lesion, the remainder 261 patients consist of 23 with head lesion and 238 with limb lesion.

In this group 21 patients with genetic disease are found, those are achondroplasia 5, bilateral short fingers 5, split hand and foot 3, Holt Oram syndrome 2, Apert' syndrome 2, osteogenesis imperfecta 1, spondylepifusial dysplasia congenita 1, hereditary arthroglyposis congenital, hereditary syndactyly 1. We are able to found 21 patients of genetic disease in 261, it corresponded to 8% in patients with head or limb lesions.

(This report supported by the Parents' association of congenital malformed child.)

B40. Frequencies of XYY and XXY Males among Juvenile Delinquents, Inpatients in Mental Hospitals and University Students: Shinichiro NANKO, Hiroshi NOMURA (Inst. Brain Res., Sch. Med., Univ. Tokyo, Tokyo) Nobuyoshi ANDO and Tadamichi MIZUKAMI (Dept. Psychiatr., Univ. Tokyo Branch Hosp., Tokyo)

X and Y chromatin survey among juvenile delinquents, inpatients in mental hospitals and university students has been undertaken. Among 1,371 male juvenile delinquents examined, 5 XYY males (0.36%) and 4 XXY males (0.29%) were found, while among 4,345 male inpatients in mental hospitals 5 XYY males (0.12%) and 21 XXY males (0.48%) were found. A XXY male was found among 1,280 male university students. The frequency of 47,XYY males among juvenile delinquents is significantly higher ($p < 0.02$) than that among newborn males (0.09%. Bell and Corey, 1974), while that among inpatients in mental hospitals is quite the same figure when compared with that among newborns. Concerning the XXY males, the frequency among inpatients in mental hospitals is significantly higher ($p < 0.001$) than that among newborn males (0.11%), while that among juvenile delinquents is quite the same figure when compared with that among newborns. These results suggest an association of character disorders with XYY but not with XXY and an association of mental disorders with XXY but not with XYY.

- B41. A Medical Study on the Etiology of Mental Retardation: Takuya IKEDA, Kenji NARITOMI, Tamotsu TERAWAKI** (Dept. Pediat., Sch. Med., Kagoshima Univ., Kagoshima), **Shozo OHDO, Yoshizumi YAMAUCHI** (Dept. Pediat., Miyazaki Med. Coll., Miyazaki) and **Hiroshi TANAKA** (Natl. Sanat. Minami-Kyushu Hosp., Kagoshima)

Although mental retardation (MR) exhibits a relatively higher prevalence which is estimated about 3% of the population, about 40% are due to unknown etiology by the previous studies.

We reported the frequency of periodic and etiologic classification, and percentage and contents of chromosomal abnormalities. Subjects were 472 children who were diagnosed MR or MR suspected by visiting each Department of Pediatrics, Kagoshima University, Miyazaki Medical College, and National Sanatorium Minami-Kyushu Hospital.

Results. 1) The frequency of periodic classification: Prenatal was most frequent, 73.7%; perinatal, 4.4%; postnatal, 0.2%. The frequency of patients who could not judge well was 21.6%. 2) The frequency of etiologic classification: (a) The most frequent cause was due to chromosomal abnormalities, 26.9%. These consisted of 133 cases of Down syndrome, 5 cases of cat cry syndrome, 2 cases of 18 trisomy, 1 case of 4p trisomy, 5q-, 7q partial trisomy, 8p+ (*de novo*), 18p-, 22 trisomy, and 48,XXYY. (b) MR due to hereditary diseases was 7.2%. 3) Clinical diagnosis was unknown in 28.4%.

- B42. Family History of Cancer in Normal Japanese Women: Motoi MURATA** (Div. Genet., Natl. Inst. Radiol. Sci., Chiba)

Familial aggregation of human cancer has been reported by many authors. But it is as yet debatable whether it is caused by the effect of hereditary factor or any environmental factors running through family members. This study was attempted to give some insight on this problem by analysing a non-random distribution of cancer family history among unaffected women.

Materials comprised about 40 thousand participants in a cervical cancer screening program in Chiba prefecture in 1977. Information on their family history was only concerned with kinds of cancer as well as kinship of their relatives who had been a cancer patient. Number of family members as well as their age distribution were not known. In addition any reported cases of cancer were not medically verified. Familial aggregation was tested by comparing observed number of combination of the diseases within a family, discriminating blood and non-blood relatives, with the expected number calculated from relative proportions of various kinds of cancer among total cases detected in all families. As a whole 4,178 and 2,903 pairs were observed for blood and non-blood relatives, respectively. For major kinds of cancer, site specific intra-familial correlation was revealed in

both and non-blood relatives. Though the former group apparently showed a stronger correlation than the latter for most cancers, the difference was not significant. When the whole population was divided into several groups according to the age (–39, 40–44, 45–) and residence (county, small city, large city) of participant themselves, familial aggregation in blood relatives was more prominent in classes of younger age and/or small city. Synergistic effect of genetic and environmental factors was suggested.

B43. Statistical Analysis on Efficacy in Potential Screening for Wilson's Disease:

Tomohiro SAITO (Dept. Environ. Health, Jichi Med. Sch., Tochigi)

The efficiency of screening for Wilson's disease by serum ceruloplasmin determination was assessed by analysing epidemiologic data in Japan.

A total of 289 affected families was collected by sending standard questionnaires to university hospitals and other hospitals from which cases were reported to medical meetings and journals. The estimated gene frequency using the Dahlberg's formula was 5.5×10^{-3} . The sensitivity of the screening test derived from the distribution of serum ceruloplasmin concentration among patients was 93% at a proposed cut-off level of 120 mg/liter. The specificity was estimated to be 99.83%. In Japan 1,500,000 children are expected to be born every year in 1980's and of these 50 would be cases of Wilson's disease. The analysis of potential screening for these children would grade three of them as false negatives and identify 2,621 as false positives. An analysis for children only from consanguineous marriages produced a more efficient result with approximately nine-fold increase in predictive value of positives and case finding rate.

Though the number of patients identified in screening for the latter high risk group is small, which is 5 out of 15,000 children screened, it is quite efficient as compared to screening for all children. It is worth considering to carry it out as a pilot study. The screening would be best done at around 2 years of age and a cut-off level placed around 120 mg/liter would be most useful.

B44. アルコール症一致, 犯罪不一致の一卵性ふたご症例: 石川文之進 (宇都宮病院),

浅香昭雄・武村信義 (東大・医・脳研), 逸見武光 (東大・医・精神衛生). **Monozygotic Twins Concordant for Alcoholism and Discordant for Criminality:** B. ISHIKAWA (Utsunomiya Mental Hosp., Utsunomiya), A. ASAKA, S. TAKEMURA (Inst. Brain Res., Sch. Med., Univ. Tokyo, Tokyo) and T. HEMMI (Dept. Mental Health, Univ. Tokyo, Tokyo)

発端者は, 56歳男子のふたごの第2子であり, アルコール症の入院歴と犯罪歴がある。ふたごの第1子は, アルコール症の入院歴はあるが, 犯罪歴はない。同胞10人(男6, 女4)中, 第7, 8番目がふたごである。同胞に大酒家はいないが, 父は大酒家であった。酩酊すると妻子に暴力をふるうなど酒乱であったが, 精神病院に入院したことはない。

発端者のふたごは、生後1週間で実父の従同胞である養父にもられ、挙子のなかった養父母の長男、嫡子として届けられている。養父は地方の素封家で人望もあり、長年町長をつとめた人格者であった。患者は、乳幼児期に著患はなく養父母に溺愛されて成長した。ふたごの相手とは幼少時はしばしば会っていたという。大学在学中に召したがすぐ終戦になり、昭和23年大学卒。昭和20年20歳時より飲酒開始。大卒後某電鉄会社につとめたが、飲酒が原因で上司とけんかし解雇された。以後職を転々とするようになるが、いつも飲酒からむトラブルが原因であった。27歳時には養父母より除籍、廃嫡にされている。現在までに精神病院入院歴は7回、通算入院期間約12年。犯罪歴としては、窃盗、強盗傷害による懲役刑が2回、婦女暴行の罰金刑などがある。離婚歴もある。

ふたごの第1子は、精神病院入院歴は4回あるが、犯罪歴はなく、現在は某公団に大過なくつとめている。

- B45. 双生児の疾病自然史に関する研究——心電図所見の症例検討：佐藤幸男・岡本直正・大前清甫・今川俊一郎・李 俊益・隅田 寛**（広島大原医研・遺伝・優生）、**安部 勉**（広島大・医・内科）、**渡辺正治**（広島大・医・社会医学）。**Natural History of Disease in Twins. Findings of Electrocardiographs: Yukio SATOW, Naomasa OKAMOTO, Kiyokazu OHMAE, Shunichiro IMAGAWA, Juung Yi LEE, Hiroshi SUMIDA** (Dept. Geneticopathol. Res. Inst., Nucl. Med. Biol., Hiroshima Univ.), **Tsutomu ABE** (Dept. Int. Med., Hiroshima Univ.) and **Shoji WATANABE** (Dept. Socio. Med., Hiroshima Univ., Hiroshima)

18歳から56歳まで9組（男7、女2組）の一卵性双生児と、9～48歳の二卵性双生児4組（男2、女2組）の臨床的、理学的諸検査の資料から、心電図、心・肺X線所見を検討して次のような知見を得た。これらの双生児の血圧および心胸比は正常範囲内にあり、臨床的に心疾患は認められていない。1) 一卵性同士のすべての組で心電図の波形、間隔、X線による心外形、動脈硬化の程度はきわめて類似しているが、二卵性では異なっていた。2) 一卵性双生児の心電図の電気軸は左方偏位の傾向を示し（平均34°、年齢平均46歳）、二卵性では平均66°、平均26歳で、対照とした24～60歳（平均44歳）までの正常血圧内の双生児ではない30症例の電気軸平均は63°であった。3) 一卵性双生児では、全例にIとaVL、あるいはIIIとaVFのR波のノッチがみられ、軽度の心室内伝導障害がみられた。

以上のノッチ波と左軸偏位を一卵性双生児の疾病自然史をみるための一つの生物学的指標とみなす妥当性、およびその普遍性について検討を重ねたい。

- B46. 双生児分裂病の臨床遺伝学的研究；分裂病の異種性および Nature-Nurture Problem を中心として：堺 俊明・広沢啓三・千原精志郎・米田 博・貞松典宏・藤田素樹・辻 敬**（大阪医大・精神神経）。**Clinicogenetic Study of Schizophrenic Twins—with Special Reference to Heterogeneity and Nature-Nurture Problem: Toshiaki SAKAI, Keizo HIROSAWA, Seishiro CHIHARA, Hiroshi YONEDA, Norihiro SADAMATSU, Motoki FUJITA, Takashi TSUJI** (Dept. Neuropsychiat., Osaka Med. Coll., Takatsuki)

従来報告されてきた分裂病の異種性の問題と、分裂病の発現における遺伝要因の問題を、われわれがこれまで集めてきた一卵性の双生児分裂病の症例28組を用いて検討した。

1) まず全例についてみると、定型分裂病と非定型分裂病との組み合わせは1組もなく、両者は遺伝的に全く独立していることを強く示唆している。次に発端者すべてを満田の分類基準にのっとり、定型群と非定型群に分け、それぞれについて一致度を比較検討した結果、定型群では完全一致8組、不完全不一致6組、非定型群では完全一致4組、不完全一致4組、不完全不一致4組、完全不一致2組となり、かなり際立った差異が認められた。また不完全不一致例の partner の示す精神症状やその性格に関しても、定型群と非定型群の間に差異が認められた。このように表現の完全なときのみならず不完全なときにおいても、その示す症状に差異がみられることは、両者が遺伝的に全く独立したものの、すなわち本症の異種性を強く示唆している。

2) 従来外国で報告された reared apart の一卵性の双生児分裂病は、わずか9組にすぎない。今回われわれは、このような症例6組を調査できたが、いま全症例15組のうち一致例は11組、不一致例は4組であった。さらに不一致例4組のうち、自験例1組はいわゆる不完全不一致であった。この結果は、分裂病の発現に際し遺伝的な要因がより重要な役割を果たしていることを示唆している。

B47. 質問紙法による双生児卵性診断の検討：浅香昭雄（東大・医・脳研）. Zygosity

Diagnosis by Use of a Questionnaire: Akio ASAKA (Inst. Brain Res., Univ. Tokyo, Tokyo)

龐大な双生児資料をあつかうときに、それらの卵性診断をメンデル形質等の遺伝マーカーを用いて行うことは、時間的にも費用の点でも不可能なことがある。すでに、スカンジナビア諸国ではほぼ同一の様式からなる質問紙票を用いて卵性診断を行い、その有効性を報告しており、実用にも供している。

そこで、同一内容の質問紙票を作成し、すでに卵性診断の確定されている双生児を対象にして、質問紙法の有効性を検討してみた。質問紙票の内容は、(1) ふたりの類似の程度、(2) ふたりが間違えられた頻度、(3) その場合誰に間違えられたか、の3項目よりなり(1)、(2)は3段階、(3)は4段階の答えが用意されており、各項目より一つずつ選択させるものである。対象は、東大附属中・高校に在学中の同性双生児より得られた MZ 78組、DZ 12組の計90組である。スコアは、段階に応じて(1)、(2)は1~3、(3)は1~4をあたえ、3項目の和を双生児の組ごとに算出した。したがって、スコアは6~20の値をとりうる。平均値は、MZ 10.6、DZ 18.3であった。14点を分割点とすると、MZは78組中76組(97.4%)が14点以下であり、DZは12組中11組(91.7%)が15点以上であった。質問紙法による卵性診断の妥当性がある程度示唆された。上記3項目を変数とした判別関数分析によっても、ほぼ同様の結果が得られた。

B48. Analysis of Infant Mortality Rate of Japanese Twins: Yoko IMAIZUMI (Inst.

Pop. Prob., Minist. Health Welf., Tokyo), Eiji INOUE (Inst. Develop. Res., Aichi Prefect. Colony, Kasugai) and Akio ASAKA (Inst. Brain Res., Univ. Tokyo, Tokyo)

In twin individuals born in Japan in the first half of 1974, rates of infant mortality up to one year of age were computed according to sex, order of birth. The rates were 5.50% for males and 3.81% for females. The lower rate for the first-born than the second-born

twin individuals indicates a reduced viability of the second-born twins, even in genotypically same MZ twins.

The effect of maternal age, gestational age and birth weight on the rates of infant mortality were also analyzed.

The rates of infant mortality of twin individuals were 4.38% and 7.76% for mothers healthy and non-healthy after delivery, respectively, and the difference is significant at the 1% level. The lowest infant mortality rate was seen in the mothers paid work during the pregnancy (4.56%) followed by the mothers engaged only in housekeeping and not working (4.72%) and self-employed during the pregnancy (4.99%). Infant mortality rate for MZ twins decreased with increased monthly expenditure on the household, whereas the rate for DZ twins was remained constant with expenditure. Socioeconomic factors still affect the infant mortality of twins, and the infant mortality rate can be improved.

B49. Study of Consanguinity in Isolated Community—Migration Pattern in To.

Village: Norio FUJIKI, Kazuo MANO (Dept. Intern. Med., Fukui Med. Sch., Fukui), Itsuro NISHIGAKI and Tohru ITO (Inst. Develop. Res., Kasugai)

We have studied the breeding structure and genetic polymorphism of To. Village, which is called Tibet in Aichi. The matrimonial migration of this village is now analyzed.

When we calculated the consanguinity rate and the mean coefficient of 97 contemporary couples with 113 children, we got 15.5% and 39.2% for first cousin marriage and consanguinity rate, respectively, and the mean coefficients were as high as 0.0156 per couple and 0.0138 per person. When we examined those of 156 couples who have ever resided in the village, we got the following figures; 12.8%, 30.8%, 0.0146, and 0.0128. When we examined the chronological change of consanguinity between 20 years before and after the World War II, the latter revealed higher consanguinity rate.

The residents within the village were more consanguineous than those who left the village. Among 63 couples who chose their partners from outside the village, 11 were consanguineous, mostly first cousin. This means that the children whose parents moved to the neighboring villages often came back to the village to get marriage to their cousins. This fact is very important for analyzing the breeding structure of the isolated community. We also compared endogamy in each generation, in parallel with the changing patterns of surnames.

B50. 同胞発症例による難病の主遺伝子の検索：安田徳一（放医研・遺伝）. Affected Sib Pair Method for Searching Major Gene in Multifactorial Disease: Norikazu YASUDA (Div. Genet., Natl. Inst. Radiol. Sci., Chiba)

疾病の遺伝素因を検索する形式遺伝学的方法は主として多因子遺伝の模型に依存しているが、疾病の遺伝力を評価するにとどまりその生理病理学的機序解明へのなかだちはほど遠い。ヒト染色体地図

作製も急速に進んでおり、メンデル性遺伝多型を標識として疾病の主効果を支配する易病遺伝子の検索も新しい方法の一つである。とくに HLA と疾病の関連の研究が進み、HLA の免疫生物学的特徴を利用して、単に遺伝というだけでなく疾病の遺伝素因も解明しうる糸口が得られるようになった。本報告では Graves 病が HLA および Gm と関連がある事実に基づき、同胞発症例を資料として Graves 症の形式遺伝学的解析を行い、この方法の有用性、限界を検討した。

HLA に関して両親がそれぞれ異なるヘテロの子供のうち、Graves 病を発症している 2 名の同胞の HLA ハプロタイプは、HLA と Graves 病に関連がなければ 1:2:1 の比で恒等なハプロタイプを 2 個、1 個、0 個保有する。実際には 27:14:2 となり、これは有意である ($\chi^2=34.30$)。HLA と Graves 病易病遺伝子が連鎖していると仮定し易病遺伝子の劣性遺伝仮説、優性遺伝仮説を検定したところ、カイ 2 乗値はそれぞれ、 $\chi_1^2=0.01$, $\chi_1^2=4.98$ となり劣性遺伝仮説が適合し、易病遺伝子頻度は 0.26 ± 0.06 となった。これは丸地ら (1969) の Graves 病発症率 0.8/1,000 と一致しない。そこで Gm と連鎖している Graves 病易病遺伝子が劣性遺伝で頻度が 0.10 という模型を考えると、浸透率も高く (0.6~1.0)、2 個の劣性遺伝子が Graves 病に関与していることが示唆された。

B51. 連鎖不平衡係数の推定法: 古庄敏行 (鹿児島大・衛生), 谷村雅子 (東医歯大・ポリポージス), 小坂樹徳 (東大・内科). **Method for Estimation of Linkage Disequilibrium Coefficient:** Toshiyuki FURUSHO (Dept. Hyg., Kagoshima Univ., Kagoshima), Masako TANIMURA (Polyposis Cent., Tokyo Med. Dent. Univ., Tokyo) and Kinori KOSAKA (Dept. Intern., Univ. Tokyo, Tokyo)

適応度の低い形質に関しては、調査の時期によりすでに淘汰を受けていることがある。

そこで集団調査資料から、適応度を考慮して連鎖不平衡係数を推定する方法を考案した。2 座位の対立遺伝子 A-a, B-b の遺伝子頻度を p, q, r, s, 連鎖不平衡係数を D, A-a 座位における各遺伝子型 AA, Aa, aa の相対的適応度を 1, 1-hw, 1-w とする。各対立遺伝子間および両座位間には任意交配、淘汰に関しては平衡状態にあるとする。以上の仮定のもとで、淘汰を考慮した連鎖不平衡係数の推定値 D は、

$$D = \alpha D_1 + \beta D_2 + \gamma D_3 + \delta D_4,$$

$$D_1 = \frac{\sqrt{S^2(1-hw)^2 + \{q(1-2hw) + hw\}^2 - (1-hw)^2 + (1-2hw)\alpha t - hws}}{1-2hw} - qs,$$

$$D_2 = \sqrt{q^2 - \beta t / (1-w)} - qs,$$

$$D_3 = \frac{\sqrt{S^2(1-hw)^2 - (1-2hw)\gamma t - hws}}{1-2hw} - qs,$$

$$D_4 = \sqrt{\delta t / (1-w)} - qs,$$

ただし、 $t = 1 - 2hwpq - wq^2$,

$\alpha, \beta, \gamma, \delta$: 各表現型 A·B-, aa·B-, A·bb, aa·bb の頻度。

以上の式をインシュリン依存型糖尿病 IDDM と HLA-Bw54 について実際のデータを補正して使い、w と h との値を動かして D の変化を調べた。w=0, h=0 のとき $D = -0.0016$ で、w=0.5, h=0.2 のとき $D = 0.000025$ であった。このように淘汰の強い形質との連鎖不平衡を調べる場合には、淘汰を考慮する必要があることがわかった。

B52. Sampling Problems in Estimation of Gene Frequency: Koji OHKURA and Tsutomu MIYASHITA (Dept. Hum. Genet. Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo)

To obtain the representative frequency of phenotype or gene of a trait in a population, the rational sampling is always the basic and important procedure. In human population study, it is obvious that the sample size is almost always restricted or limited by several reasons. In this case, there no suitable sampling method is provided, slightly different samplings often cause district difference of gene frequency.

We observed the differences of the gene frequencies of PGM and Hp in Korean populations caused by various sampling methods. In this study we used 1,088 individuals that has been analyzed the phenotype of both PGM and Hp. The samples are arranged in order from number 1 to number 1,088. And 1/2 samples are sampled, for example, No. 2, No. 4, No. 6,... or No. 1, No. 3, No. 5,... and so on. We observed the wide differences of the gene frequency of PGM which ranged from 0.7399 to 0.7822. The difference of the lowest value from the highest is 0.0423. And also, the gene frequency of Hp changes from 0.7022 to 0.7215. The difference of the lowest and the highest is calculated as 0.0193. All gene frequencies estimated satisfy the Hardy-Weinberg's equilibrium, so we are waved in choice which value is the representative one.

Because the value of the gene frequency is so different, the two samples are often seem to be the different populations when the values of PGM and Hp are compared in the same time. The same results are obtained when 1/3 samples are selected from 1,088 samples. It can be concluded that a single sampling could not reveal the representative gene frequency.

- C1. Dermatoglyphic Patterns of the Kabuki Make-Up Syndrome: Norio NIKAWA, Yoshimitsu FUKUSHIMA (Dept. Pediat., Hokkaido Univ. Sch. Med., Sapporo), Yoshikazu KUROKI, Yasuyuki SUZUKI, Ichiro MATSUI (Div. Med. Genet., Kanagawa Child. Med. Cent., Yokohama) and Tadashi KAJII (Dept. Pediat., Yamaguchi Univ. Sch. Med., Ube)**

Dermatoglyphic analyses of 12 patients with the newly recognized kabuki make-up syndrome revealed a combination of unusual dermatoglyphic patterns. They included frequent fingertip ulnar loop patterns (72%), the absence of digital triradius c or d (25%), an interdigital triadius bc or cd (33%), hypothenar loop patterns (67%), and ulnar loop patterns in the fourth interdigital area (17%). Other unusual findings included persistence of fingertip pads (58%), a single flexion crease of the fourth or fifth finger (25%), and an excess of minor flexion crease of the palm (92%).

- C2. Hallermann-Streiff 症候群の一例: 渡辺 章・仲田教子・星野映治・石飛和幸・原田義道 (鳥取大・医・三内). A case of Hallermann-Streiff Syndrome. Akira WATANABE, Noriko NAKATA, Eiji HOSHINO, Kazuyuki ISHITOBI and Yoshimichi HARADA (3rd Dept. Intern. Med., Tottori Univ., Yonago)**

Hallermann-Streiff 症候群はおうむ様顔貌, 減毛症, 低身長, 小眼球症, 先天性白内障, 皮膚の萎縮性変化, 歯牙の異常などの胎内における外胚葉性および中胚葉性の発育異常を主症状とする先天性疾患である。今回われわれはその一例を報告し, 文献的考察を加えた。

症例は16歳女, 低身長を主訴とし, 当科受診。母体妊娠中異常なく, 満期頭位安産, 生下時身長50 cm, 体重2,950 gで, 生後3ヵ月ころより視力の低下に気づかれ盲学校へ入学したが, その他既往歴, 家族歴に特記事項を認めなかった。現症では身長130.3 cm (−5.1σ), 体重35 kgで小顔面, 前側頭部禿, 眉毛睫毛希薄, 小眼球, 水平眼振, とがった鼻, 一部歯牙の先天性欠損を認め, また乳房, 恥毛発育はTanner分類でIV度, II度であった。眼科的には遠視, 水晶体欠損あり, 虹彩は萎縮性であった。検査では検尿, 血液一般で異常なく, また血液生化学でも異常を認めなかった。末梢血染色体分析は46,XXで正常。内分泌学的検査では, GH分泌, TRH test, LH-RH test, Metirapone testとも年齢相当の反応を認めた。本症候群は文献上内外合わせて75例を集計し, そのうち男36例, 女39例で, 父娘例, 双生児例, 染色体異常の報告もあるが, 大部分は突然変異による散発例であった。François・positive signsではおうむ様顔貌100%, 先天性白内障96%, 歯牙の異常83%, 減毛症75%, 小眼球症73%, 皮膚萎縮68%, 均衡性小人症57%, の順で高い陽性率が認められた。

- C3. A Family of Familial HDL Deficiency (Tangier Disease): Haruki NAKAMURA, Katsuhiko HAYASHI, Michio FUKUMA, Nobuyoshi TACHIBANA, Kazunori TSUDA (2nd Dept. Intern. Med., Miyazaki Med. Coll., Miyazaki), Nariaki MIYAMOTO (Miyazaki Univ., Miyazaki) Hideo MAEDA and Haruo UZAWA (Kumamoto Univ. Sch. Med., Kumamoto)**

This patient is a 30 year-old female who has been under treatment by the psychiatry service in our hospital for manic-depressive illness. She was referred to our service be-

cause of recent onset of palpitation. Physically, irregular pulses, slightly cloud cornea and hepatosplenomegaly were observed, whereas no enlarged tonsils, enlarged lymphnodes or neurological abnormalities were observed. The laboratory findings were as follows: total cholesterol 66 mg/dl, chol. ester ratio 71%, HDL chol. less than 1 mg/dl, triglyceride 145 mg/dl, phospholipid 100 mg/dl, lipoprotein fraction α 0%, pre β + β 100% (floating β band), apo A-I 2.3 mg/dl, apo A-II 6.3%, ultracentrifugal analyses of plasma lipoproteins-absent HDL. Microscopic examination of the liver revealed scattered depositions of the fat in the hepatocytes and a number of masses of the foam cells in the sinusoids. These foam cells have features of Kupffer cells under the electronmicroscopic study. The examination of her family members revealed that her parents were cousins and her elder sister had complete HDL deficiency.

The familial HDL deficiency (Tangier disease) is reported to be autosomal recessive in inheritance and 28 homozygotes over 22 families have been reported in literature. This may be the first case reported in Japan. The further analysis of this disease will lead us to understand an important role of the HDL function in human.

C4. Monozygotic Triplets with Rare Gc Variant in Common: Hideo MATSUMOTO, Tasuku TOYOMASU, Kiyoshi MATSUI (Dept. Legal Med., Osaka Med. Sch., Takatsuki) and Hiroyuki MAKIHARA (Dept. Psychiat., Hyogo Coll. Med., Nishinomiya)

In case of the zygosity test of the triplets, one of whom was in-patient in the diagnosis of schizophrenia and two of them were out-patients in the same diagnosis, rare Gc variant phenotype was found in common among the triplets. Eleven red blood cell groups (ABO, MNSs, P, Se, Rh, Kell, Kidd, Duffy, Lewis, Lutheran, and Diego), six serum protein groups (Hp, Tf, Gm, Km, Gc and Pi), and eleven red cell enzyme groups (AP, PGM, ADA, PGD, EsD, s-GPT, s-GOT, PHI, GLO and UMPK) have been investigated for the triplets (female, aged 18) including the elder sister, their parents, and paternal grand father. The triplets were diagnosed as monozygotic in the probability of 99.99% because of the identity for all of the blood groups investigated. Rare Gc variant phenotype with rare allele Gc^{2A4} was observed in common among the triplets and it was confirmed that the triplets have inherited the allele through their father from paternal grand father.

C5. Genetic Variants of the Human Diaphorase DIA₃ in the Japanese: Ismail M. SEBETAN, Suguru AKAISHI (Dept. Forens. Med., Tohoku Univ., Sendai) Tasuku TOYOMASU and Hideo MATSUMOTO (Dept. Legal Med., Osaka Med. Sch., Takatsuki)

Sperm-lysates from 124 unrelated Japanese males were tested for the polymorphism of the human diaphorase DIA₃ by isoelectric focusing in thin-layer polyacrylamide gels over

pH 3.5-9.5 gradient. An additional third common allele was identified in our population samples and the estimated allele frequencies for the commonly encountered phenotypes, *i.e.* DIA_3 1-1, 2-1, 3-1 and 2-2, were: $DIA_3^1=0.839$, $DIA_3^2=0.141$ and $DIA_3^3=0.020$. The observed and expected values provide a good fit to the Hardy-Weinberg equilibrium.

C6. Isoelectric Focusing Studies of PGM_1 Polymorphism in Japanese: Itsuro NISHIGAKI, Tohoru ITOH (Dept. Genet., Inst. Dev. Res., Aichi Prefect. Colon., Kasugai), H.-G. BENKMANN and H.W. GOEDDE (Inst. Hum. Genet., Hamburg Univ., Hamburg)

The use of thin-layer polyacrylamide isoelectric focusing has led a more complex exhibition of PGM_1 which each of the isoenzyme products of PGM_1^1 and PGM_1^2 could be further distinguished into two subtypes. Although a finding of this new technique followed a possibility for an even better applicability of this polymorphic system, due to an increased occurrence of mating chance for different alleles at the PGM_1 locus, most of isoelectric focusing data hitherto have been reported on samples from Caucasian populations. In this study we examined, therefore, the distribution of the PGM_1 subtypes by isoelectric focusing on 218 Japanese samples. Nine common phenotypes were observed corresponding to the following frequencies of the four alleles at the PGM_1 locus: PGM_1^{1+} 0.6560, PGM_1^{1-} 0.1170, PGM_1^{2+} 0.1674, and PGM_1^{2-} 0.0505. Comparing with data from other ethnic populations, the quantity for PGM_1^{1+} (0.6560) calculated in Japanese was demonstrated to range between the two levels of Caucasians and Africans, showing a close value to the former.

In addition, a characterization of the PGM_1^7 allele, which might occur in a polymorphic proportion in Japanese, was performed. Our results revealed a possibility that the PGM_1^7 allele may be differentiated in the two alleles of PGM_1^{7+} and PGM_1^{7-} through an investigation of isoelectric focusing. Although only the PGM_1 7-1 phenotype with PGM_1^{7+} was detected in this survey, a convincing evidence for our supposition might be obtained by an observation of the PGM_1 7-1 phenotype with PGM_1^{7-} .

C7. Polymorphism of Properdin Factor B in Japanese. Description of A Rare Variant: Katsushi TOKUNAGA, Keiichi OMOTO (Dept. Anthropol., Univ. Tokyo, Tokyo), Hirao MAEDA (Blood Transfus. Serv., Tokyo Univ. Hosp., Tokyo), Takeo JUJI (Blood Transfus. Serv., Tokyo Women's Med. Coll., Tokyo), Shuntaro ISHIBA and Hiroshi MARUYAMA (Dept. Pediat., Tokyo Women's Med. Coll., Tokyo)

Polymorphism of the properdin factor B (BF) was investigated in 496 unrelated healthy adult Japanese and in 65 Japanese patients with insulin-dependent diabetes mellitus (IDDM).

Besides the phenotypes reported previously in Japanese (S, FS and F), two rare heterozygous phenotypes (tentatively named FTS and FTF) were observed. A single individual with this rare type was found in healthy controls, while two individuals, one FTS and the other FTF, were found in IDDM patients. The allele frequencies for BF^*S , BF^*F , and BF^*FT (F Tokyo) in healthy Japanese were estimated to be 0.799, 0.200, and 0.001, respectively.

The relative electrophoretic mobility of the FT band was measured to be F0.80. The conversion fragment Bb of the variant phenotypes showed a double banded pattern. BF hemolytic activities of the variants were roughly at the same level as other common phenotypes. The incidence of BF FT factor was significantly higher in IDDM patients than in normal controls, while of BF F decreased significantly in patients.

C8. Genetic Polymorphism of the B Subunit of Human Coagulation Factor XIII:
Yoshio KERA, Hiroaki NISHIMUKAI and Kichihei YAMASAWA (Dept. Legal
Med., Kyoto Prefect. Univ. Med., Kyoto)

Recently, genetic polymorphism of the B subunit of factor XIII (factor XIII-B) in an Australian population (Board, 1980) was reported. It was described that there were three codominant alleles ($F-XIIIB^1$, $F-XIIIB^2$ and $F-XIIIB^3$) at an autosomal locus, but no individual with phenotype 2-2 was reported.

By using the agarose gel isoelectric focusing and immunofixation, we tried to examine the genetic trait of factor XIII-B. In the isoelectric focusing profile of factor XIII-B, three different groups of the pattern, tentatively designated 'F', 'S' and 'FS', were observed. The isoelectric points of 'F', 'S' and 'FS' were pH 5.1–5.4, pH 5.3–5.6 and pH 5.1–5.6, respectively. The 'FS' had 4 or 5 major and 3 or 2 minor bands, and appeared to be superimposition of patterns in 'F' and 'S'. Several pattern-variations in each group (F_1 , F_2 and F_3 in 'F' group, S_1 , S_2 and S_3 in 'S' group) were observed. Those patterns of F_1 (or F_2), F_3 , FS, S_1 , S_2 and S_3 seemed to be similar to those of 1-2, 1-1, 1-3, 3-3, 2-3 and 2-2 in the previous report (Board, 1980), but those pattern-variations were not obtained from desialylized samples with neuraminidase. Furthermore, in the family study, some cases that the inheritance mode could not be interpreted without application of two allelic model were encountered. All results in the present study may suggest that factor XIII-B phenotypes (F, S and FS) are primarily controlled by the two codominant alleles ($F-XIIIB^F$ and $F-XIIIB^S$) as structural gene on an autosomal locus, and are modified by the sialic acid. Allele frequencies of $F-XIIIB^F$ and $F-XIIIB^S$ in a Japanese population were 0.336 and 0.664, respectively.

C9. Genetic Polymorphism of the A Subunit of Human Coagulation Factor XIII in Japanese: Hiroaki NISHIMUKAI, Yoshio KERA and Kichihei YAMASAWA
(Dept. Legal Med., Kyoto Prefect. Univ. Med., Kyoto)

Human coagulation factor XIII, the precursor of the enzyme fibrinoligase, is normally present in blood as the inactive form. The factor XIII isolated from plasma consists of two A and two B subunits (A_2B_2) linked together by non-covalent bonds. The A subunit has the enzymatic activity and the B subunit serves as a carrier molecule in plasma (Schwartz *et al.*, 1973).

Genetic polymorphism of the A subunit of factor XIII (factor XIII-A) has been discovered in an Australian population using agarose gel electrophoresis followed by immunofixation or a specific transglutaminase staining technique (Board, 1979).

The present paper described the study of genetic polymorphism of XIII-A in a Japanese population, using the method of agarose gel isoelectric focusing and immunofixation. The isoelectric focusing patterns of factor XIII-A were classified into three types. One type (1-1), commonly observed in Japanese population, had an acidic single band with the pI value ≈ 5.64 , and another type (2-2) had a basic single band with the pI value ≈ 5.76 . The remainder (2-1) had both acidic and basic bands and an additional intermediate band. The inheritance of factor XIII-A types was studied in 55 families. Three phenotypes were expressed not by the sex-linked alleles but by two codominant alleles; $F-XIIIA^1$ and $F-XIIIA^2$ on an autosomal locus. Allele frequencies of $F-XIIIA^1$ and $F-XIIIA^2$ in Japanese population were 0.900 and 0.100, respectively.

C10. A Case of *de novo* 8/18 Translocation Resulting in 18q Trisomy: Mashio KITATANI, Junya YASUDA, Norimasa SERA, Takako MATUDA, Keiso TACHI and Hiroaki TAKAHASHI
(Dept. Pediat., Kanazawa Med. Univ., Ishikawa)

Clinical findings. The proband was the second child of 26-year-old healthy mother by 40 weeks of gestation. Pregnancy and delivery were uneventful. Birth weight was 2,650 g. At age 1 month the child was hospitalized because of intermittent cyanosis, feeding difficulties and malformations. Moderate growth retardation was noted (wt: 3,008 g; ht: 50 cm). The following malformations were observed: prominent occiput, malformed ears, prominent nasal bridge, high arched palate, micrognathia, webbed and short neck, polydactyly, single crease on fifth fingers, overlapping and webbed fingers, simple arches on 9 fingertips, rocker bottom feet, hypoplastic nails and incurved fourth toes. Cardiac catheterization revealed VSD and PPS. CT scanning revealed ventricular dilatation. Routine laboratory studies were normal. Family history was negative. Father (31-year-old) and sister (4-year-old) were in good health. There was no consanguinity. There was no spontaneous abortion.

Cytogenetic findings. Karyotyping was performed on cultured peripheral lymphocytes after trypsin-Giemsa staining and acridine orange staining. One chromosome 8 was missing and an abnormally large chromosome with the following configuration was present: 8qter→8p23::18q11→18qter. The propositus thus presents trisomy 18q11→qter and monosomy 8pter. Parental karyotypes were normal.

C11. XXXX Syndrome. Case Report and Findings of CT-Scanning: Hiroyuki CHO, Toyojiro MATSUSHI, Yasuyuki EZAKI, Shigeru KARUKAYA (Dept. Pediat., Kurume Univ., Kurume), Masazumi TAKENAKA (Dept. Oral Surg., Kurume Univ., Kurume), Tsukasa IRIKI and Yukari KUMA (Kurume Natl. Hsop., Kurume)

More than 20 cases of tetra X syndrome had been reported. EEG abnormality was commonly observed in these cases. We presented a case of 48,XXXX female with abnormal CT-scanning findings.

Case (80-1493): Proband was the second child born to healthy unrelated parents. At the time of birth, the father was 33-years-old and the mother 30. There was no history of drugs, infections, or radiation during the pregnancy. Birth weight was 2,737 g (gestation; 39W.). Mile-stones were slightly retarded: Controlled her head at 6 months of age, walked alone at 22 months, spoke several words at 25 months. There had been no episode of seizures. EEG examined at the age of 2 years was normal. Abnormal behavior was noticed: She tore her hair with her hand. She had sudden general tonic convulsion and apnea without fever and was admitted to the hospital at the age of 3 and 4/12 years. Physical examination revealed no growth retardation. She had unusual appearance due to frontal bossing, high-arched palate, epicanthus and plumpy face. The abdomen was moderately dilated. The external genitalia had normal shape. Blood analysis showed moderate anemia (Hb; 9.1 g/dl). Blood chemistry was not remarkable. Gonadotropins in the blood were slightly elevated (FSH; 31 mIU/ml, LH; 7.3 mIU/ml). X-ray examination of the teeth showed taurodontism and congenital absence of the teeth. (543 | 345). Dermatoglyphic findings were not characteristic; Total ridge count was 172 and atd angles were 57° (left palm) and 67° (right palm). CT- brain scanning demonstrated mild to moderate ventricular enlargement, EEG showed irregular spike and wave complex. The karyotype of peripheral blood was analyzed using G-banding technique. Buccal epithelial cells with 3 X-chromatins were observed. The karyotype of the proband was 48,XXXX. Abnormal findings of EEG and CT-scanning might indicate congenital defect of CNS of the patient with tetra X syndrome.

C12. Y-22 Translocation with Germ Cell Tumor: Katsuhide IMAIZUMI, Katsumi HISHIDA, Kaoru SUZUMORI, Kin-ichiro MIZUNO, Yoshiaki YAGAMI and Takako HISAOKA (Dept. Obst. Gynec., Nagoya City Univ., Nagoya)

Translocation of the Y chromosome to the autosome has been reported very rarely. We represented the investigation of a phenotypic female with cytogenetically identified Y-22 translocation. A 16-years-old girl consulted our hospital for abdominal tumor and primary amenorrhea. She had an unremarkable medical and family history. Physical examination revealed that her height was 144.5 cm and her weight 45.8 kg. Scalp hair was distributed normally but there was no facial, axillary or pubic hair. The neck was not webbed, and the carrying angle of the elbow was not increased. The breast development was very poor. Surgical exploration was performed, with right gonadectomy. Gross examination of right gonad revealed a 18×16 cm tumor, but left was streak. Histopathologic finding of this tumor was consistent with germ cell tumor like dysgerminoma. Peripheral blood cell culture was done for the chromosome analysis following the R-, G-, Q- and C-banding techniques. Although all metaphases showed 45 chromosomes, there were two different types of cells, one with 45,X,t(Yq; 22q), and the other 45,X. In about 96% of the cells investigated, 45,X,t(Yq; 22q) was present, and in the remaining cells 45,X was observed. The karyotype of this patient was designated as a mosaicism of 45,X,t(Yq; 22q)/45,X. The H-Y antigen expression was determined by the Goldberg's method, and the H-Y antigen level of this patient represented the normal male level.

C13. Cytogenetic Study on Sixty Couples with Recurrent Abortions: J. EDAGAWA, M. TANIWAKI, Y. YAMANE,* Y. SONODA, T. IDE, S. MISAWA, T. ABE, T. TAKINO (Dept. Med., *Clin. Lab., Kyoto Prefect. Univ. Med., Kyoto) and K. HAYASHI (Dept. Obst., Kyoto Univ. Sch. Med., Kyoto)

During the years 1976-1981 sixty couples who had episodes of more than two spontaneous abortions were cytogenetically investigated. For the analysis conventional G-banding and also in some cases high-resolution G-banding techniques were used. Translocation carriers-both reciprocal and Robertsonian- were found in six couples (10%), which was somewhat higher when compared to the results reported recently by several authors. Chromosome constitution of the present six cases were as follows: 45,XY,t(13; 14) (p11; q11) (two cases), 46,XX,t(1; 11) (q23; q25), 46,XY,t(4; 10) (p16; q24), 46,XX,t(6; 7) (q25; q11.2), and 46,XX,t(6; 10) (q21; q25). In the same 5-year period eight translocation carriers were also identified among individuals who had been referred to us because they had produced chromosomally disabled children and/or because of another reasons. Balanced chromosomal rearrangements included 45,XX,t(14; 21) (p11; q11) (two cases), 46,XX,t(2; 21) (p11; p11), 46,XX,t(4; 17) (q25; p13), 45,XX,t(13; 14) (p11; q11), 46,XY,t(3; 6)

(p13; p23), 46,XX,t(2; 3) (q37; q25), and 46,XX,t(1; 21) (q25; q22). Therefore, it was concluded that the habitual abortion was found in about one half of all translocation carriers excluding D/21 translocation carriers, though overall frequency of the latter cases was uncertain. According to the method described by Daniel (1979), relation of the grade of chromosome imbalance to the abortion and the unbalanced live-birth was studied and discussed.

C14. A Case of 11q Trisomy: Nobuaki IWAYA (Dept. Psychiat., Hyogo Coll. Med., Nishinomiya), Hideaki CHIYO, Tomoko HASHIMOTO, Jun-ichi FURUYAMA (Dept. Genet., Hyogo Coll. Med., Nishinomiya), Sachiyo DOI (Dept. Cent. Lab., Hyogo Coll. Med., Nishinomiya), Megumu MIYAKE (Palmore Hosp., Kobe), and Masahiro NAKAYAMA (Dev. Pathol., Osaka Med. Cent. Women Child., Osaka)

A case of 11q trisomy was presented. The proband was born to 35-year-old healthy mother at 37 week gestation. He weighed 2,760 g at birth and main clinical findings were as follows; round face, hypertelorism, broad and low nasal bridge, long philtrum, high arched palate, micrognathia, low set ears, short neck, small scapulae, abnormal position of the limbs, wide set nipples, small penis, rocker bottom feet. Chromosome study revealed the proband had the karyotype of 46,XY,der(2),t(2; 11) (p25; q13) and his mother as a translocation carrier. The proband died at the age of 1 year of severe congenital heart disease (ASD+PS+PDA). The necropsy showed many types of congenital cardiovascular anomalies and malrotation of intestine. For the present, about 20 cases of 11q trisomy were reported in the world. The clinical features of these cases were very similar and it is agreeable that 11q trisomy would constitute a clinical as well as a cytogenetic syndrome.

C15. A Female Infant with Trisomy 20p: Shigeru KARUKAYA, Makado MATSUYUKI, Yuuko SHIOTSUKI and Hirohisa KATO (Dept. Pediat., Kurume Univ., Kurume).

The abnormalities in the F-group chromosome are rare in Japan, and few cases of the confirmed chromosome 20 have been reported. This report deals with a case of the trisomy of the short arm of chromosome 20. The patient is an 8-month-old girl born as the second child in the third pregnancy to the nonconsanguineous, healthy parents, 33-year-old mother and 32-year-old father. The first child, 6-year-old female, is healthy. There was a history of spontaneous abortion in the second pregnancy in this couple, during the third pregnancy, the mother had no toxemia of pregnancy, radiation, drug administration and viral infection. The patient was born at 40th gestational week, with the birth weight

of 3,300 g. She required resuscitation because of grade asphyxia. At the age of 8 months, she could smile, but head control had not been achieved.

The abnormalities found were: reddish sparse hair, deformity of the skull, flat right occiput, peculiar facial appearance, upward slanted palpebral fissures, flat nasal bridge, large philtrum, protruding tongue, low set ears, deformed auricles, short neck, umbilical hernia, bilateral 2/3 syndactyly on foot, large 4th finger on the right hand, tetralogy of Fallot, patent ductus arteriosus, patent foramen ovale, right simian crease, t' axial tri-radius on the right hand and an abnormal shadow over the right lung field (this phenomenon is not clear). Each of these clinical features may not necessarily be related to the chromosomal aberration, because the patient has cerebral palsy, a sequela of neonatal asphyxia, to which some of the features may be ascribed.

Chromosome preparation was made by the standard method from the culture of peripheral blood lymphocytes. Chromosomal identification was carried out by means of G-banding. Analysis was carried out on C- and Q-banding and silver stained preparation. Karyotype of the patient's chromosomes determined by G-banding method showed a 46,XX,-15,+der(15),t(15;20)(cen;cen)mat in all cells examined. This 15/20 translocation chromosome was inherited from the patient's mother, who had a 46,XX,t(15;20)(15qter→15cen::20cen→20pter;20qter→20cen:), and was phenotypically normal. Elder sister's karyotype was identical with that of her mother. Her father was chromosomally normal.

C16. Diploid/Tetraploid Mixoploid in a Case of Live Born Female: Miyako YABUKI,¹ Hideaki CHIYO,² Hiromi SAKAMOTO,² Tomoko HASHIMOTO,² Jun-ich FURUYAMA,² Norimitsu OHTSUKA,³ Susumu TSUJI,⁴ Reiko OZAKI,¹ Hiroyoshi WADA,¹ Hideo MATSUMOTO⁵ and Hiroshi HARA⁶ (¹Dept. Pediat., Hyogo Coll. Med., ²Dept. Genet., Hyogo Coll. Med., ³Dept. Cent. Lab., Hyogo Coll. Med., Nishinomiya, ⁴Dept. Pediat., Hanwa Hosp., Osaka, ⁵Dept. Legal Med., Osaka Med. Coll., Takatsuki, ⁶Div. Blood Transfus., Hyogo Coll. Med., Nishinomiya)

A case of diploid/tetraploid mosaicism was demonstrated. Proposita was 1-year-old female infant who was born to a healthy 35-year-old mother at 37 week gestation. Both the pregnancy and delivery were uneventful. She weighed 2,095 g at birth. Main clinical features were as follows; small and round face, hypertelorism, small nose, micrognathia, cleft palate, low set ears, slender and short extremities, overlapping fingers, pes varus, large clitoris. At 1 year of age, she weighed only 4,500 g (-5 SD) and could not sit or crawl.

Routine chromosome study revealed about 85% of tetraploid cells in peripheral blood. In born marrow cells and skin fibroblasts, such tetraploid cells could not be found. Other

cytogenetic studies including the study of heteromorphic chromosomes and polymorphism, suggested that the polyploidy would be resulted from a failure of division in one of diploid cells at the early stage of the cleavage.

C17. Two Cases of 3q Trisomy: Noriko HIRAYAMA (Dept. Pediat., Nissei Hosp., Osaka), **Keiko YUMURA** (Dept. Pediat., Osaka Univ. Hosp., Osaka), **Hideaki CHIYO**, **Hiromi SAKAMOTO**, **Tomoko HASHIMOTO** (Dept. Genet., Hyogo Coll. Med., Nishinomiya), **Sachiyo DOI** (Dept. Cent. Lab., Hyogo Coll. Med., Nishinomiya), **Masaru NISHIDA** (Dept. Pediat., Osaka Prefect. Hosp., Osaka) and **Minoru IMADA** (Dept. Pediat., Nissei Hosp., Osaka)

Case 1. Proposita was 3-month-old female infant. Main clinical findings were as follows; congenital heart disease (VSD+PH), microcephalus, upward slanting eyeballs, hypertrichosis nose, high-arched palate. Chromosome study revealed the proposita and her father as 46,XX,rec(3),dup q,inv(3) (p26q26) and 46,XY,inv(3) (p26q26) respectively.

Case 2. Propositus was born to 24-year-old mother. At 39 week gestation, a Caesarean section was performed because of bradycardia of the fetus. He weighed 2,350 g at birth, and died at 22 days of age with heart failure (VSD). Main clinical findings were as follows; square shaped face, bulbous nose, micrognathia, hypertrichosis, slender and short extremities, hypospadias. His karyotype was 46,XY,der(3),t(3; 5) (q13; p14)mat.

The clinical features of these 2 cases seemed to be a little different each other. The monosomy for the terminal region of short arm of No. 3 chromosome was strongly suspected to influence the phenotype of Case 1.

C18. Partial Trisomy 2p: Ken HAYASHI, **Kenji IDA** (Dept. ObGyn., Kyoto Univ., Kyoto), **Kazuyo MITSUDO**, **Mutsuo TANAKA** (Dept. Pediat., Kurashikichuo Hosp.) and **Akihiko UKITA** (Dept. ObGyn., Kurashikichuo Hosp., Kurashiki)

Partial trisomy 2p has been reported in 18 cases including 3 in Japan. Our case is one year and three month old male whose cousin is also partial trisomy 2p complicated with neuroblastoma and reported by Nagano *et al.* at the 23rd meeting of The Japan Society of Human Genetics. The parents are 30 (mother) and 31 (father) years old. After a 40-weeks pregnancy without complication, delivery was normal, with Apgar score 7, birth-weight 2,320 g, height 46.2 cm, and forehead circumference 32.5 cm. Clinical examination revealed frontal bossing, flat, wide glabella, and nasal bridge, maxillary hypoplasia, small penis, and retention testis. He had weak sucking ability, frequent occurrence of fever and lethargy. He showed very low TBG count, extraordinarily high T_3 -RSU, and normal free T_4 count. He also had mental retardation and hypertrophic myocarditis, and a year after the birth, he showed infantile spasm-like seizure which was improved by the ACTH therapy.

Close chromosomal banding analysis of the peripheral lymphocyte revealed that the patient's karyotype was 46 XY, -16, +der(16)t(2; 16) (p13; p11)pat, karyotype of the father 46 XY,t(2; 16) (2q ter→2p13 :: 16p11→16p ter; 16q ter→16p11 :: 2p13→2p ter) and karyotype of the mother who is now pregnant 46,XX. The result of amniocentesis showed the fetus was a normal male.

C19. A Case of Partial Monosomy 6p: Kazunobu OUCHI (Dept. Pediat., Natl. Okayama Hosp., Okayama) and Ryoza KASAI (Asahigawa Jidoin Child. Hosp., Okayama)

We here report a case of partial deletion 6p, which has not been reported before. A female new-born was admitted to Natl. Okayama Hosp. because of asphyxia. Her mother was 29 years old and her father 34. They and her two sisters have been healthy. Family history was not contributory. She was born after 39 week normal gestation, weighing 2,360 g. The following abnormalities were noted at admission. Large anterior and posterior fontanels, prominent occiput, hypoplasia of right ear lobe, atresia of right external acoustic meatus, low set of both ear lobes, left accessory ear lobe, cleft lip and palate, micrognathia, short neck, exceed nuchal skin, hypoplasia of nipples, funnel chest, small external genitalia, clinodactyly of both fifth fingers, and hypotonia. Dermatoglyphic analysis showed that archs were prominent on both fingers and palm triradius was t'. At the age of 5 months she died of heart failure. Necropsy revealed single ostium of coronary arteries, abnormal tricuspid and mitral value, membranous aneurysmal dilatation of ventricular septum, ovarian cysts, and right hydronephrosis. Chromosomal analysis of peripheral lymphocytes by standard technique (G band) showed partial deletion 6p and karyotype was 46,XX,del(6)(23). Chromosomes of both parents were normal. Her HLA typing was identical with parents' HLA typing, suggesting that HLA gene is located at more proximal portion than 6p23.

C20. 21 モノソミーを示した猫なき症候群: 山中 昂 (愛知県コローニ中央病院・小児), 大石英恒 (愛知県コローニ発達障害研・遺伝), 小笠原信明 (愛知県コローニ発達障害研・生化), 津田克也 (津田こどもクリニック), 荻野高敏 (名古屋市大・小児). Apparent 21 Monosomy in a Female Infant with Cri du chat Syndrome: Tsutomu YAMANAKA, Hidetsune OISHI, Nobuaki OGASAWARA (Cent. Hosp., Inst. Dev. Res., Aichi Prefect. Colon., Kasugai), Katsuya TSUDA (Tsuda Clin., Seto) and Takatoshi OGINO (Dept. Pediat., Nagoya City Univ., Nagoya)

症例は1979年8月25日生まれの子供、妊娠中には異常なく、在胎39週、生下時体重1,500gのSFDであった。出生時父29歳、母29歳の第3子で、同胞2人は健康である。生後すぐ、総合病院の新生児センターに収容され、2ヶ月間入院していた。生後1週目ころよりチアノーゼが出現、心雑音も聴取され諸検査の結果、ファロー四徴症と臨床診断された。多発奇形のため染色体検査をうけ、

G モノソミーを指摘され、紹介にてコロニー中央病院を受診した。

初診時 (1 歳) 体重 6.13 kg, 身長 72 cm と発育障害があり, 高口蓋, 両眼分離, 丸い顔, 小顎症, 弱々しい泣き声などから猫なき症候群を疑った。BrdU-AO 法による R バンド染色で, 欠失しているのは 21 番目染色体であることが判明した。完全な 21 モノソミーかどうかを調べるため, 21 番目染色体 q22 に遺伝子座がある superoxide dismutase-1 (SOD-1) の酵素活性を測定したところ, 両親・患児とも正常な活性を示した。よって少なくとも q22 部分は欠失してないと考えられた。また, 5 番目染色体 p13 は欠失しておらず, 臨床像で猫なき症候群を疑わせることより, 患児の核型は, 45,XX, -5, -21, +der(5)t(5;21)(p14;q21) と診断した。両親の染色体は正常だった。こうした一見 G モノソミーを示す猫なき症候群は, 文献的にこれまでに 5 例の報告があった。なお, 患児は急性心不全にて, 1 歳 6 カ月で死亡した。

C21. A Rare Chromosome Aberration in a Male Child with Congenital Anomalies and Stereotypy: Shigeru KARUKAYA, Shigenori YUKIZANE (Dept. Pediat., Kurume Univ., Kurume), Miwako TSUNOSUE (Dept. Pediat., Chikugo City-Hosp., Chikugo) and Yukari KUMA (Clin. Lab., Kurume Natl. Hosp., Kurume)

This male patient was admitted to the "A" institution because of the abnormal behaviors (stereotypy), and he was referred to the Dept. of Pediatrics (O.P.D) of City-Hosp., Chikugo. Clinical examinations revealed that he had mental retardation congenital anomalies and a chromosome aberration.

The patient was a 3-year-old boy, born in the second pregnancy. He was the product of 39 week's pregnancy, born as the first child to the nonconsanguineous parents, 28-year-old healthy mother and 26-year-old father. The father had been diagnosed as having depression. The mother had a history of artificial abortion in the first pregnancy, and spontaneous abortions in the third. During pregnancy of the propositus, the mother had an episode of threatened abortion but no history was elicited for radiation, viral infections, drug administration and toxemia of pregnancy. The birth weight was 3,350 g and asphyxia (grade unknown) was noticed at birth. He had weak sucking and cry, funicular hernia 8 h after birth, and inguinal hernia at 7M of age, and he was operated on for phimosis at 9M of age. Cyanotic episodes recurred 3 times about 10 months of age, when fever and equivocal convulsions were noticed. He was admitted approximately at 2 years of age because of leukocytosis. He achieved head control at 6th months, rolling over at 5M, sitting at 7M, standing with support at 18M, standing at 30M, walking at 36M and one word speech at 17M.

Clinically, mental retardation, stereotypy, moderate EEG abnormalities and brain atrophy were especially evident in this child. Other abnormalities involved were peculiar facial appearance, frontal bossing, high palate, long philtrum, bilateral coloboma iridis, cubitus valgus, polydactyly, funicular hernia, inguinal hernia, phimosis and small penis. Dermatoglyphic findings revealed axial triradii (t''), hypothenar pattern (L) and simian

crease (R).

The chromosome investigation was done only in this patient. Chromosome analysis by the G-, T- and Q-banding techniques on peripheral blood lymphocytes showed chromosome number 47 with a translocation between Nos. 2 and 5 chromosomes and a G-like marker chromosome; 47,XY,t(2p-;5q+),+mar. In this case, the mechanism of the occurrence of chromosomal aberration was unknown.

C22. The Study of the Patients with a Small Extra Chromosome. 1. A Case of Partial 22 Trisomy: Naoki NOMOTO (Dept. Pediat., Kyoto City Hosp., Kyoto) and Osamu NAGAUCHI (Dept. Clin. Lab., Kyoto City Hosp., Kyoto)

We have experienced 6 patients with a small extra chromosome during the past 10 years. These chromosomes were not identified by G-staining method.

We reported a case of partial 22 trisomy, which was diagnosed by Q- or R-staining methods and patient's phenotype. This extra chromosome was shown as a small satellite acrocentric chromosome on G-bands and confirmed on C-bands or NORs. Its long arm fluoresced palely on Q-bands and intensely on R-bands. Therefore, we concluded that the extra chromosome originated in chromosome No. 22. The patient's karyotype was 47,XY,+del(22)(q11). We investigated the origin of the extra chromosome. The findings of Q- or C-bands and NORs suggested that the extra chromosome might be derived from his mother.

The patient was a 5-year-old male, whose clinical features included; moderate mental and developmental retardation, antimongoloid slant, hypertelorism, low nasal bridge, micrognathia, high arched palate, large ears, slight ear malformations, dimple at root of r-helix, and exposed glans. The eyes, extremities, and visceral organs appeared normal. Computed tomography of the brain revealed mild enlargement of interhemispheric fissure and bifrontal subdural spaces, and mild ventricular dilatation. His weight was 16.4 kg, length 105.1 cm, head circumference 51.8 cm, and chest circumference 55.8 cm. He held head up at 6 months, sat up at 11 months, and walked at 2 years of age. He first spoke some words at 3 years of age.

He was the product of a full term pregnancy born to a 27-year-old woman (gravida I, para O). His father was 33-year-old at his birth. His birth weight was 2,240 g, length 43.5 cm, head circumference 31 cm, and chest circumference 28 cm. The phenotypes and karyotypes of both parents were normal.

Dermatoglyphic study showed palmar axial triradius in the t'' position, loop in the 3rd interdigital areas, A_u/A_c in the hypothenar patterns, and all whorls in the digital areas, bilaterally. On the soles, hallucal areas had loop distal bilaterally.

C23. ヒトT-cell line (ALL) 由来 X 線高感受性株ならびに X 線抵抗変異株の核型の差
 異: 田口尚弘・白石行正 (高知医大・解剖). **The Difference of Karyotypes in Human T-Cell Lines with X-Ray Sensitive and Resistant Characters:** Takahiro TAGUCHI and Yukimasa Shiraishi (Dept. Anat., Kochi Med. Sch., Kochi)

X 線感受性に差のある同じ T-cell line 由来細胞株において、X 線感受性について調べた。材料には、ALL 患者由来 T-cell line の CCRF-HSB₂(HSB₂): 46,XY, t(1;7)(p32;q32) と、それから spontaneous に分離された CCRF-HSB₂-M (M): 47,XY, t(1;7)(p32;q32), +t(6;6)(p11;q13), t(12;16)(q24;q11), -16, +22 を使った。

HSB₂ は、すでに cell killing と染色体異常の点から、X 線高感受性であることが知られている。この M line は HSB₂ 由来にもかかわらず X 線の cell killing に対し、正常株と同じくらいに抵抗性となっていることが見出された。さらに X 線の染色体異常の効果について調べると、照射後 12 hr では、HSB₂ も M も正常株に比し約 2 倍の頻度で見られた。24 hr でも同様であった。12 hr 後 HSB₂ より M は chromatid delution (cd-del) の頻度がかなり高い。しかし、chromosome delution (ch-del) は同レベルであった。24 hr 後では HSB₂ の ch-del の頻度が M より高い。これら両 lines の X 線による cell killing の効果の差は、ch-del の頻度と両者の核型の差により生じていると思われる。しかし、ch-del は M line でも control (Normal line) に比べかなり高いのは注目される。また HSB₂ は X 線照射後の caffeine (1.0 mM) 添加により、その生存率が X 線単独のものより上昇する傾向が見出されている。この現象も正常細胞の複製後修復を caffeine は阻害するという作用に反するもので、X 線高感受性となんらかの関係があると思われる。

C24. Pierre-Robin 症候群の症例に認められた 11 番染色体長腕部分欠失低頻度モザイシズム: 笠井良造 (旭川児童院), 橘原幸二・木本 浩 (岡山大・医・小児), 井上英雄 (岡山済生会総合病院・小児). **Low-Percentage Mosaicism of 11q Interstitial Deletion in a Newborn with Pierre-Robin Syndrome:** R. KASAI (Asahigawa Jidoin Child. Hosp., Okayama), K. NARAHARA, H. KIMOTO (Dept., Pediat., Okayama Univ., Okayama) and H. INOUE (Dept., Pediat., Saiseikai General Hosp., Okayama)

症例は新生児女児。在胎 41 週、出生体重 2,820 g。母親 27 歳、父親 29 歳のとき出生。妊娠、分娩異常なし。アプガースコア 7 点。分娩直後より呼吸困難、チアノーゼを示した。理学所見として Pierre-Robin 症候群 (小顎症、口蓋裂、舌根沈下) および両側猿線が認められた。生後 3 日目に肺拡張不全のため死亡。剖検では、副脾を除き内部臓器に異常なし。末梢血リンパ球の染色体検査で、分析した 141 個の細胞のうち 135 個の細胞では 46,XX で正常であったが、6 個の細胞に 11 番染色体長腕中間欠失 46,XX, del(11)(q23q23) がみられ、低頻度モザイシズム (4.3%) と考えられた。

11q- 症候群は特徴的な表現型異常を示すが、本症例では mosaicism のために奇形が軽度であったと思われる。また、本症例のような低頻度モザイシズムの存在は、多発奇形を示す症例の染色体検査において、分染法による分析細胞数を増加させる必要性、あるいは皮膚線維芽細胞を同時に分析する必要性を示唆している。

C25. Three Cases of Partial Tetrasomy 15q Identified by Distamycin A/DAPI Staining: Kouji NARAHARA, Yoshifumi KODAMA, Shunsuke KIMURA, Hiroshi KIMOTO (Dept. Pediat., Okayama Univ., Okayama), Ryoza KASAI (Asahigawa Jidoin Hosp., Okayama), Masahiro KATAYAMA and Hideo INOUE (Dept., Pediat., Saiseikai General Hosp., Okayama)

Supernumerary bisatellited G-group-like chromosomes have been shown to be preferentially derived from chromosome 15, and they are designated as inv dup(15) (pter→q1 :: q1→pter) (Schreck *et al.*, 1977). We presented 3 unrelated cases with inv dup(15) identified by Distamycin A/DAPI staining.

Case 1, a 7-year-old girl, had profound mental retardation, hyperkinetic behavior, short stature, saddle nose, and congenital dislocation of the right hip joint. Case 2, a 27-year-old boy, had severe mental retardation, hypokinetic behavior, epileptic seizures, short stature, and ear malformations. Case 3, a 5-year-old boy, had moderate mental retardation, abnormal speech development, latent epilepsy, microcephaly and visual disturbances due to congenital retinal folds.

In all the cases, Distamycin A/DAPI staining revealed subterminal fluorescence on each arm of the supernumerary chromosomes. On the basis of the G-, Q-, C- and N-banding patterns, the constitution of the chromosomes were interpreted as being inv dup(15) (pter→q13 :: q13→pter). The chromosome abnormality in Case 3 was transmitted from the father with subnormal intelligence but no other phenotypic abnormalities.

It is noteworthy that cases with inv dup(15) lack specific phenotypic abnormalities. The main clinical manifestations are mental retardation, behavior disorders and epileptic seizures. The difference in the clinical picture between each case may be explained by the variation in the fine structure of inv dup(15). Familial transmission of inv dup(15) is exceedingly rare, and only one such case has been so far described (Power *et al.*, 1977). The presence of familial transmission, however, provide important implications for genetic counseling of the families.

Inv dup(15) is considered to be structurally dicentric but functionally monocentric. In each of the 3 cases, this chromosome was mitotically stable. Although the number of satellite associations on the short arm was nearly as many as on the long arm of the chromosome, Ag-staining intensity was always more pronounced on the long arm. This would afford an information for the mechanism of the selective centromeric inactivation in this chromosome.

- C26. Smoldering Leukemia を発症した 18 番染色体短腕欠失の 1 症例：吉川清志・橋原幸二・木村俊介・小田 慈・永瀬 恵・木本 浩(岡山大・小児), 尾崎 寛(香川県立中央病院). Smoldering Leukemia in a Case of 18p Deletion Syndrome: Kiyoshi KIKKAWA, Kouji NARAHARA, Shunsuke KIMURA, Megumi ODA, Kei NAGASE, Hiroshi KIMOTO (Dept. Pediat., Okayama Univ., Okayama) and Hiroshi OZAKI (Kagawa Prefect. Cent. Hosp., Kagawa)**

症例は女児。母に 2 回の自然流産の既往あり。胎生 35 週, 生下時体重 2,060 g, 父親 30 歳, 母親 30 歳のとき, 第 2 子として出生。乳幼児期の発達は正常。4 歳のとき, 汎血球減少をきたした。白血病細胞は末梢血に出現していなかったが, 骨髄細胞の 19% に認められ acute lymphoblastic leukemia と診断された。化学療法により完全寛解を得, 現在 9 歳で再発はみられない。染色体核型は, 46,XX, del(18)(p11) で, 理学所見として低身長, 大きく聳立した耳介, 長い人中, 小さい口, 被髪部低位, 外反肘, 翼状頸が認められた。知能障害は比較的軽度であった。両親の核型は正常。免疫学的検査では, IgA と natural killer activity の低下がみられた。

染色体異常症で白血病を発症する場合, acute non-lymphocytic leukemia が多く, 先天性白血病, 著明な好酸球増多の合併あるいは aplastic anemia に続発するなど特殊な発症様式をとることが特徴である。本症例は ALL type で, aleukemic leukemia の発症様式をとったことは興味深い。

- C27. Partial Trisomy of Long Arm of Chromosome 2: Hiromi SAKAMOTO, Jun-ichi FURUYAMA (Dept. Genet., Hyogo Coll. Med., Nishinomiya), Fumihiko IKOMA (Dept. Urol., Hyogo Coll. Med., Nishinomiya), and Norimitsu OHTSUKA (Dept. Cent. Lab., Hyogo Coll. Med., Nishinomiya)**

Since the first case of the partial trisomy of long arm of chromosome 2 was described by Ricci *et al.* in 1968, about 10 cases with the same chromosome aberration have been reported. We experienced a case with trisomy of long arm of chromosome 2 (2q31 → 2qter) derived from paternal translocation. The propositus was a girl born July 5, 1978. Her birth weight was 2,200 g, length 45 cm. Caesarian operation was needed for her birth at 42 weeks gestation. She was the first child between 25-year-old mother and 30-year-old father. Her mother had two spontaneous miscarriages. She had been addmitted for 1 year owing to her poor sucking ability. At her discharge, her weight was 5,670 g (−3.4 SD), length 64 cm (−3.9 SD). She could hold her head by 1 year old, turn herself by 2 years old. She suffered from recurrent pyelonephritis. She referred to the department of urology in Hyogo College of Medicine. She had square face, protruding forehead, Mongoloid slanting palpebral fissures, strabismus, hyperterolism, short nose, broad nasal bridge, split nose, low-set deformed ears, thin mouth lips with turned down corners, high-arched palate, micrognathia, short neck, short and tapering fingers, clinodactyly of the 5th fingers, and immature dermal ridges. Chromosomal examinations of the patient and her parents were performed. Mother had normal karyotype. Father had a balanced

translocation between chromosome 2 and 11. Karyotype of the patient was identified to be 46,XX,-11,+der(11),t(2;11)(q31;q25)pat.

C28. An Unusual Case of Polycythemia Vera and Diabetes Mellitus Associated with Klinefelter's Syndrome: Eiji HOSHINO, Noriko NAKADA, Akira WATANABE, Osamu NOZAKI, Kazuyuki ISHITOBI and Yoshimichi HARADA (Dept. Int. Med., Tottori Univ., Yonago)

Myeloproliferative diseases including leukemia have been repeatedly reported in the patients with Klinefelter's syndrome, but the association of this syndrome and polycythemia vera seems to be rare, and only one case of it is seen in the literature. The present patient, born in 1913, was diagnosed to have diabetes mellitus following detection of glycosuria at age 50. The patient was put on a diabetic diet initially, and has been treated with insulin since age 65. At age 64, he was noted to have conjunctival injection and erythema of the skin, and was referred to our clinic because of high blood count at age 65. He has been married since age 26, but has no children. There is no record of consanguinity or infertility among his immediate relatives. On admission, October, 1978, his height was 171.3 cm, weight 61 kg and arm span 175.5 cm. The following signs of Klinefelter's syndrome were noted: small testes (2.5×1.5 cm on both), gynecomastia, cubitus valgus, simian crease and diminished axillary and pubic hair. Hematological examination revealed erythrocytosis (RBC 938×10^4 /cmm) and leukocytosis (WBC 12,400/cmm). On bone marrow examination erythroblastic hyperplasia was observed. Serum iron was 46 μ g/dl, serum vitamin B₁₂ was higher than 3,200 pg/ml, and leukocyte alkaline phosphatase score was 286. Blood sugar was 287 mg/dl and 50 g OGTT showed a diabetic pattern with no response of immunoreactive insulin. Treatment with phosphorus-32 was given in January, 1979 for polycythemia vera without remission. Busulfan, 4 mg daily, was given from October, 1980 to July, 1981, following which RBC and WBC decreased to normal levels. Prior to the treatment, all 21 bone marrow cells studied had a 47,XY,+C karyotype. All 100 cells examined from a lymphocyte culture showed a 47,XXY karyotype following G-banding technique: Among them 9 cells showed gaps and breaks in No. 1, 8 and 20 chromosomes. Buccal smears showed a single X-chromatin body in 26 out of 100 cells. After the therapy in July, 1981, 47,XXY karyotype was determined as before, and breaks and gaps in No. 1, 8, 9 and 20 chromosomes were observed in about 30% of cultured lymphocytes.

C29. A Case of Mosaic 5p- Syndrome: Noriko NAKADA, Osamu NOZAKI, Akira WATANABE, Kazuyuki ISHITOBI and Yoshimichi HARADA (Dept. Intern. Med., Tottori Univ., Yonago)

A 14-year-old girl with mosaic 5p- syndrome is reported. The patient was born as a product of normal pregnancy and delivery, being the 2nd child of a 28-year-old mother and a 34-year-old father. At her birth, the weight was 2,650 g and the height 45 cm. She was diagnosed as having atresia ani and rectovaginal fistula, and was suspected to have atrial septal defect during the infant period. She underwent colostomy at age 7 months and was operated on for right inguinal hernia at age 6. The artificial anus was closed at age 7. She received treatment of paralytic ileus and recurrent benign hematuria at age 13. The cat-like cry has not been noticed since her birth. There is no consanguinity in the parents nor congenital diseases in her family tree. The patient was referred to our clinic because of short stature and amenorrhea at age 14.

On physical examinations she was 129 cm (-4.5σ) tall and weighed 28 kg. She had no secondary sex characters and showed small head, round face with hypertelorism and epicanthus, short neck with webbing, and pigmented nevi. She has been doing very poorly at school.

Urinary excretion of 17-KS was 1.3 mg/day and serum estradiol was 34.4 pg/ml. Serum LH and FSH in the basal state were 16.6 mIU/ml and 5.5 mIU/ml respectively, and these hormones showed normal response to intravenous LH-RH. Serum levels of thyroid hormones, TSH, GH, and PRL were all within normal ranges.

Her EEG appeared to be slightly abnormal and her ECG showed incomplete right bundle branch block. X-ray examinations demonstrated bone age of 12 years, hypoplasia of the right first rib and normal intravenous pyelogram. Dermatoglyphs showed simian lines and hypothenar patterns on both hands and a total finger ridge count was 192.

Lymphocyte cultures were established for chromosome studies from the patient and the parents. The parents had no chromosomal abnormalities. In the patient the modal number of chromosomes was determined as 46, but in detailed karyotypic analysis by G-banding method, a deletion of 5p14 was detected in 24 metaphase cells, and 61 cells showed a normal 46,XX karyotype. Thus, the patient was a mosaic of 46,XX/46,XX, del(5p14) (72%/28%).

C30. 核型 46,XX,psu dic(18)(qter→cen→p11.32;p11.32→qter) を示す 18—トリソミー症候群の 1 例：池内達郎（東医歯大・細胞遺伝），内藤達男（国立小児病院・新生児）. A Case of 18—Trisomy Syndrome Showing a Karyotype 46,XX,psu dic(18)(qter→cen→p11.32;p11.32→qter): Tatsuro IKEUCHI (Dept. Cytogenet., Tokyo Med. Dent. Univ., Tokyo) and Tatsuo NAITO (Natl. Child. Hosp., Tokyo)

症例は、重症仮死の未熟児（生下時体重 1,400 g）として、健康な両親（母 35 歳，父 36 歳）より出生した女兒。妊娠時、羊水の過多・混濁が認められた。身体所見：後頭部隆起，耳介の低位と変形，鼻背隆起，鉤鼻，小顎，口蓋裂，両手第 2 指と第 5 指の屈曲，両手猿線，爪形成不全，足の拇趾短く背屈，外性器異常（陰核肥大など）。生後 25 日目に死亡し，次のような剖検所見が認められた。食道閉鎖，先天性心疾患（心室中隔欠損，動脈管開存症，大動脈縮窄症），馬蹄腎，総腸間膜症，鎖肛。

染色体検査には，PHA-媒介による末梢血培養および EB ウイルス感染により樹立したリンパ芽球細胞株を用いた。通常の Q- および G- 染色法により，No. 18 染色体の短腕に過剰部を認めた。両親の核型には異常は認められなかった。患児にみられる異常 No. 18 の過剰部の分染パターンは No. 18 長腕部のそれと類似しており，C- 染色法を施したところ，動原体部の C- バンドのほかに，過剰部を有する短腕側の両染色分体に 1 個ずつの C- バンドが検出された。このことから，異常 No. 18 は二動原体性で過剰部の動原体は不活化されている psu dic (18) であることがわかった。さらに，臭化エチジウム前処理法による G- バンドの高精度解析を行った結果，dic (18) の分染像は短腕末端部（p11.32, ISCN 1981 の命名規約による）を中心として完全な対称形を示しており，したがって患児は No. 18 の大部分に関してトリソミーであることが判明した。患児の上記臨床知見は 18—トリソミー症候群のそれとよく合致する。

C31. New Techniques for the Chromosome Identification Using Actinomycin D, Distamycin A, Chromomycin A₃ and DAPI: M. Taniwaki, K. Nishida, S. Tsuda, T. Maekawa, J. Edagawa, Y. Sonoda, T. Ide, S. Misawa, T. Abe and T. Takino (Dept. Med., Kyoto Prefect. Univ. Med., Kyoto)

Bone marrow cells from two patients with AML and a patient with CML, and PHA-stimulated lymphocyte from two patients with congenital anomaly were subjected to this experiments. Methods by which various bandings were obtained are as follows: 1) *AMD/DAPI staining*. Slides were stained for 15 min with AMD (0.25 mg/ml, McIlvaine buffer pH 7.0), then rinsed with buffer, and stained for 5 min with DAPI (0.2 μg/ml, McIlvaine buffer pH 7.0). 2) *CMA₃/DMA staining*. Slides were stained for 40 min with CMA₃ (0.5 mg/ml), to which MgCl₂ (10 mM) was added, then briefly rinsed with buffer, stained with DMA (0.01 mg/ml) for 15 min. 3) *DMA/DAPI staining*. Slides were stained for 15 min with 0.01 mg/ml DMA and subsequently stained with DAPI (0.2 μg/ml) for 5 min.

46,XX,r(18), 46,XX,inv(9), t(7; 9; 11) (q11; q14; p11) and t(9; 22) (q34; q11) were clearly demonstrated. R-bands using CMA₃/DMA and C-bands with DMA/DAPI were induced without any distortion, which were inevitable by the alkali-denaturation procedure of conventional R- and C-banding methods. In addition, consecutive induction of R-, C- and Q-bands on the same metaphase plate was possible, which contributed to precise

analysis of marker chromosomes by fluorescence of heterochromatic regions of Nos. 1, 9, 15, 16 and Y after staining with DMA/DAPI. These new methods reported here have some advantage of sparing time and higher effectiveness. This work was supported in part by a grant from the Ministry of Education, Japan.

C32. The Determination of the Sites of Sister Chromatid Exchanges (SCE) by G-Banding Method: Hachiro SHIMBA, Kazuo OHTAKI and Akio A. AWA (RERF, Hiroshima)

The present study was undertaken to determine the precise location of sister chromatid exchange (SCE) sites by the two-step staining technique (G- and FPG-methods) in cultured lymphocytes from a healthy donor. Blood samples were cultured for 72 hr in MEM medium containing 10 μ g/ml BudR. Chromosome slides were treated with a 0.4% pancreatin solution for about 1 min, and G-banded metaphases were first photographed. After analysis of the G-banded preparations the slides were de-stained, treated with Hoechst 33258 for 15 min, and then exposed to UV-light for about 30 min (FPG method). The slides were finally re-stained with Giemsa solution. This two-step staining technique allows us to compare the G-banding pattern with the SCE pattern in the same metaphases.

Of 216 cells analyzed, 37, 76 and 103 cells were identified as being in their first, second and third *in vitro* cell divisions, respectively. Of the 76 cells at the second *in vitro* mitosis, 693 SCEs were scored (9.1/cell), and 1,206 SCEs (11.7/cell) in 103 cells at the third mitosis. A further observation was made to analyze the SCE frequency in each chromosome, based on the assumption that the number of SCEs (observed values) is proportional to the length of individual chromosomes (expected values). A chi-square test showed that there was a significant statistical difference between expected and observed values; the SCE frequency was higher in no. 2, no. 3 and no. 8 chromosomes in cells at the second cell division than expected, and also in no. 1, no. 2 and no. 4 chromosomes in cells at third cell division. In contrast the frequency of SCEs in no. 17 chromosomes and in chromosomes of F and G groups in cells at both the 2nd and 3rd cell divisions was lower than expected. The most frequent exchange sites were shown to be at 1q32, 3q21, 4q31 and 6q21. G-banding analysis indicated that most of SCEs seemed to occur at negative bands.

C33. S.R.L. における染色体異常の出現頻度と種類: 高橋桂子・横沢拓郎・海井秀之 (財) S.R.L. 染色体)

1980年1月から1981年6月までの18ヵ月間に、全国から染色体検査のため、当社に依頼された検体の中で、20細胞以上分析可能であった7,788件について、検査を実施した。方法としては、末梢血リンパ球培養法および分染法 (G, Q, C-banding) を用いた。

総検査数のうち1,783件について異常が確認され、それらの異常検体数を、性染色体異常 (439件)

と常染色体異常 (1,344 件) に大別し、それぞれの出現頻度等について分類した。総検査数における異常率は、22.89% (1979 年, 24.79%), 性染色体では、5.65% (5.34%), 常染色体では、17.24% (19.45%) であった。このように、1979 年度の統計と比較検討の結果、異常率においては、ほぼ同率の値が得られた。

1979 年度から始めた統計処理も、今回で 2 度目となり、今後も継続していきたいと思う。