

ABSTRACTS OF ORIGINAL ARTICLES (IN JAPANESE
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Abstracts of Original Articles

1. Clinical Studies on the Pulse Wave Velocity, Especially the Diagnostic Significance of Arteriosclerosis

Ryoichi BIZEN

(1st Dept. Internal Medicine — M. Komiya)

The pulse wave velocity of 63 normal subjects, 45 arteriosclerotic patients with hypertension, 17 arteriosclerotic patients without hypertension and 5 patients with juvenile hypertension was measured by the Strain-Gauge method of digital plethysmography. The pulse wave velocity was found to increase with age, but there was no significant difference between sexes in normal subjects.

The pulse wave velocity was significantly greater than in normal subjects even in the arteriosclerotic patients or hypertensive patients, being the greatest in the arteriosclerotic patients with hypertension. In the patients belonging to the second degree group according to Scheie's classification of arteriosclerosis, there was a positive correlation between the pulse wave velocity and the blood pressure.

The rate of decrease of the pulse wave velocity was compared between the arteriosclerotic patients with hypertension and in patients with juvenile hypertension, when the blood pressure fell after the administration of anti-hypertensive drugs. The rate of decrease of the pulse wave velocity in patients with juvenile hypertension was significantly greater than that in arteriosclerotic patients with hypertension.

In comparing the pulse wave velocity with the eyeground findings, Scheie's classification of hypertension and Keith-Wagner's classification were found to be significantly correlated with the pulse wave velocity, but Scheie's classification of arteriosclerosis was not significantly correlated with the pulse wave velocity.

In diabetic patients, the pulse wave velocity of those with arteriosclerosis or hypertension was distinctly greater, but the pulse

wave velocity of those without arteriosclerosis or hypertension was within normal limits. In cases over 50 years of age, there was found no difference between the pulse wave velocity of the diabetic patients and that of the arteriosclerotic patients and the hypertensive patients.

2. The Clinical and Experimental Study on Serum Enzymes in Lung Cancer

Masaaki KANAYAMA

(2nd Dept. Internal Medicine — S. Ōbuchi)

The purpose of the present work was to determine the activities of aldolase (ALD), β -glucuronidase (β -gl), lactic dehydrogenase (LDH); malic dehydrogenase (MDH) and phosphohexoisomerase (PHI) in serum of 23 patients with lung cancer and 13 patients with other lung diseases, and to observe the effects of chemotherapy and radiation therapy on these serum enzymes and correlation between these enzymes and clinical findings. In addition, the author determined the activities of these enzymes in serum, tumor tissue and liver of lung tumor bearing rats induced by infusion of 20-methylcholanthrene into lung with tracheal tube.

Serum ALD increased in 9 of 18 cases with lung cancer and in 1 of 12 cases with other lung diseases. Serum β -gl increased in 8 of 19 cases with lung cancer and in 4 of 11 cases with other lung diseases. Serum LDH increased in 14 of 23 cases with lung cancer but none of 13 cases with other lung diseases. Serum MDH increased in 5 of 16 cases with lung cancer but none of 10 cases with other lung diseases. Serum PHI increased in 8 of 17 cases with lung cancer and in 2 of 12 cases with other lung diseases. The increase of LDH activities was most remarkable and most specific in lung cancer when compared to other lung diseases.

These serum enzymes mostly decreased at 2 weeks after chemotherapy or radiation. In serum of 20-methylcholanthrene induced

lung tumor bearing rat, these enzymes increased. These enzyme activities were higher in the experimental lung tumor tissue than in normal lung tissue. There was not any difference between experimental lung tumor bearing rats and control rats in liver ALD, LDH and transaminase activities.

3. Evaluation on the Sulfonyl-urea D860 in the Therapy of Diabetes Mellitus

Yasuo SUGIYAMA

(1st Dept. Internal Medicine — M. Komiya)

Glucose tolerance test and insulin sensitivity test were performed in 23 normal persons and 50 diabetic patients, before and after the treatment with B860 or insulin.

Blood glucose level was more rapidly elevated by ingestion of carbohydrate and prolonged at higher level in the diabetic than the normal. There was no significant difference in improvement of diabetes in the treatment with D860 and insulin, so far as the glucose tolerance was concerned.

Insulin sensitivity index ranged from 1.26 to 2.46 by statistic analysis in the normal persons. In the diabetic patients, insulin sensitivity index under the normal was encountered in 8 cases, within normal range in 22 cases and above the normal in 20 individuals.

The abnormal insulin sensitivity index became normal by both therapy, and there was no difference of the improvement of the insulin sensitivity value in both treatments. The treatment with D860 as well as insulin resulted in the improvement of not only blood glucose but also hormonal balance in diabetes.

4. A Modified Determination of Urinary Pregnanediol and Physiological Variation of the Metabolite in Women

Kunihiko SUGATA

(Dept. Gynecology — K. Fujii)

Klopper's method for determination of urinary pregnanediol, which was accepted to

be one of the most common procedure, was studied and modified in some processes as follows.

1. As an eluate of first column-chromatography 0.5% Et-Benzene, instead of 0.8% solvent in the original method, was used in the present experiment.

2. Pregnanediol fraction was acetylated with acetic anhydride, not with acetylchloride.

3. The original procedure was carried out at the room temperature. In the present experiment a prompt color reaction with sulfuric acid was observed by heating at 100°C.

Previously to the column-chromatography, alumina was deactivated to 3.5 degree of the Brochman scale. With this modified method, human urinary pregnanediol excretion was determined under various condition including physiological.

In the present experiment a linear calibration curve was obtained. Recovery was increased to 80% in average (70%: original method).

5. Clinical Application of Gestagens and Their Effects on the Urinary Pregnanediol

Kunihiko SUGATA

(Dept. Gynecology — K. Fujii)

It was previously mentioned that our modified method was much easier for pregnanediol acetylation than Klopper's originals. To be described in the present paper is a clinical application of our modified method.

A. INHIBITING EFFECTS OF VARIOUS GESTAGENS ON THE OVULATION.

Gestagens used in the present experiment were norethynodrel, 19-norethisterone, chlormadinone, lynestrenol and B.D.H. 1928. The gestagens were daily given to 41 normal women from 5- to 25-day after the menstruation. Basal body temperature was daily recorded. Effects of the gestagens were detected by urinary pregnanediol level, vaginal smear, cervical mucus and urinary gonadotropin level. Inhibitory effects on the ovulation were evidently observed by all of the

gestagens and the effects continued throughout the administration period of 3 months.

B. ATTEMPT TO PROLONG THE LUTEAL PHASE.

Attempt to study an influence of administration of prolactin in combination with H.C.G. on the corpus luteum was made. If prolactin was given alone, an evident stimulation to the corpus luteum could not be found. In the case of H.C.G. alone, a sufficient dose might stimulate the corpus luteum. The effect of H.C.G. was increased by combination with prolactin.

C. EFFECT OF 6,21-DIMETHYLETHISTERONE ON THE PREGNANCY.

In the present experiment influences of gestagens on the internal secretion of the pregnant women was studied. Twenty normal pregnant women were divided into two groups; early- and late-pregnancy. Urinary pregnanediol was determined by our previous mentioned method after the daily administration of 6,21-dimethylethisterone for 7 days to each group. Urinary pregnanediol was decreased in almost all of the materials. No disturbances in both the pregnancy and the delivery were found.

6. Experimental Study on Broncho-pulmonary Changes in Vitamin-A Deficiency

Kiyoo SHIOIRI
and

Keikichi MITSUNAGA

(1st Dept. Internal Medicine — M. Komiya)

It is the well-known fact that various factors such as smoking, air pollution play an important part in the pathogenesis of chronic bronchitis. The part of endogenous factors, however, remains unresolved. Vitamin A is one of such endogenous factors with affection on bronchial epithel.

Some histopathological observations of the changes of bronchopulmonary system were performed in adult rat with vitamin A deficient diet.

Following results were obtained.

1) Such characteristic changes such as

untidy hair and eyes abnormality due to V.A. deficiency were observed at the terminal stage after about 100 days trial.

2) Broncho-pulmonary changes were found much more in either V.A. deficient group or forced smoking group than control, and the most severe in double loading (both V.A. deficient diet feeding and forced smoking group.)

3) Squamous metaplasia or keratinization of bronchial epithel were scanty, while, inflammatory and emphysematous changes were rather prominent in adult rat with V.A. deficiency.

4) Bronchial lesions due to forced smoking showed a tendency to improve in 30 days after cessation of smoking, but such tendency were little in V.A. deficient group and double loading group.

7. On the So-called Myxoma of the Heart in a Pig

Homare OHTANI, Takuro YOSHIDA,
Takeshi KINOSHITA

(Dept. Public Health, Azabu Veterinary College — T. Yamada)

Kenji NAMIE and Kazuo TAKEMOTO
(Dept. Public Health — H. Maeda)

The myxomatous tumor was found on autopsy in a 2 years-old female pig in Inuyama Abattoir, Aichi Prefecture.

This tumor was identifiable with those reported as myxoma of the heart in man and the case report has not be published in pigs.

This tumor was found in the left atrium. The gross and microscopical features pointed to the conclusion that this tumor was a true mesenchimal neoplasm and not organized thrombi.

8. Ca^{++} -dependent Adenosine Triphosphatase Obtained from Erythrocyte Membranes and Microsome Fraction

Yohtalou TASHIMA

(Dept. Biochemistry — M. Nakao)

A preparation which had ATPase activity was obtained by treatment of microsome fraction and erythrocyte membranes with 2M LiI. The preparation hydrolysed nucleoside triphosphates and ADP. The ATPase activity required Ca^{++} which was substituted by Mg^{++} , and was inhibited by monovalent cations more strongly with increasing the ionic strength. Its properties including pH optimum, distribution among various tissues and subcellular fractions, and inhibition by ouabain were quite different from the two ATPases obtained from erythrocyte membranes, one of which was the ATPase stimulated by Na^+ and K^+ , and the other was stimulated by Na^+ or K^+ (T. Nakao *et al.*, Biochem. Biophys. Res. Commun., **13**, 444; 1963).

9. The Effect of Irradiation on the Metabolism in Isolated Nuclei of Rat Bone Marrow

Kazuhiro MIYAZAKI

(Dept. Biochemistry — M. Nakao)

The effect of *in vitro* X-ray irradiation upon the phosphate metabolism of isolated nuclei and upon nuclear deoxyribonucleic acid complex from rat bone marrow was examined.

The nuclear suspension exposed to 200r X-ray was immediately incubated at 2°C or 3.7°C under various conditions, e.g., with or without glucose, adenine plus inosine, or under aerobic or anaerobic conditions, and its content of easily hydrolysable phosphate or ATP was determined.

Slight but statistically significant difference ($P=0.001$) was present between the content of energy-rich phosphate of the irradiated and control nuclear suspension. More distinguished effect was observed after irradiation of the extracted deoxyribonucleic acid

protein complex, its viscosity drop being far more rapid in the irradiated extracts. The result suggests that the primary effect of small dose X-ray irradiation on the nuclear metabolism is the disruption of deoxynucleo-protein complex.

Several sulfur containing compounds, glutathione, mercaptoethylamine, sodium thio-sulfate, sodium sulfite, protected the viscosity drop after irradiation.

Several other reducing reagents, ascorbic acid or α -tocopherol were ineffective.

10. Experimental Study on the Pathogenesis of Erythropoietic Depression of Chloramphenicol

Kiyoo SHIOIRI

(1st Dept. Internal Medicine — M. Komiya)

Erythropoietic depression has recently been reemphasized following administration of chloramphenicol but the exact mechanism of this time- and dose-dependent change is unknown. Accordingly, a study was undertaken to investigate the capacity and mode of action of chloramphenicol to suppress erythropoiesis in experimental animals. Chloramphenicol was administered intraperitoneally to d-d mice and its depressive effect on erythropoiesis was determined by utilizing the 24-hour incorporation of ^{59}Fe into red cells as a parameter.

A negative correlation was observed between the dosage and ^{59}Fe incorporation when chloramphenicol, ranging from 0.4 to 40 mg daily, was injected for three days ($r=-0.91$, $p<0.05$), on the other hand, 10 mg chloramphenicol given in a single dose did not cause any significant depression of erythropoiesis ($p>0.05$). These results indicate that the inhibitory effect of chloramphenicol on erythropoiesis in mice is dependent on its dose and duration of treatment.

In the next series of experiments, six injections of chloramphenicol were given every 12 hours simultaneously with the human urine containing a high erythropoietin activity, which prevented erythropoietic depression due to chloramphenicol, thereby the higher the erythropoietin titer of the urine was, the more pronounced protection of ery-

thropoiesis was seen ($r=0.98$, $p<0.05$). Mice injected with chloramphenicol and subjected to hypoxic stimulus, however, were not protected from erythropoietic depression ($p>0.05$) in spite of the fact that plasmas of the mice contained a high erythropoietic activity as shown by bioassay in polycythemic mice ($p<0.05$). It is suggested that suppression of chloramphenicol on erythropoiesis *in vivo* is either mediated by a decrease in the production of "activated" erythropoietin or caused by an inhibitory effect on the site of action of erythropoietin.

Further investigations are being done in an attempt to elucidate the relation of chloramphenicol to the production and action of erythropoietin.

11. A Survey of 3 Tumors Collected from Animals Slaughtered for Food

Homare OHTANI, Takuro YOSHIDA,
Takeshi KINOSHITA

(Dept. Public Health, Azabu Veterinary
College — T. Yamada
and Kenji NAMIE

(Dept. Public Health — H. Maeda)

Among 42,448 pigs slaughtered in Inuyama Abattoir (Aichi Pref.) during the past 3 years (1963–1966), 3 tumors were found.

They were diagnosed as the embryonal nephroma, the myxoma of the heart and the chondroma.

In this report, the gross, microscopical features and the incidence were discussed.

12. On the Carbonic Anhydrase Activity of Uterus of the Rabbit

Kazuo ARAI

(Dept. Gynecology — K. Fujii)

The carbonic anhydrase activity of the rabbit uterus was investigated following the treatment with various gestagens, during pseudopregnancy and gestation, and under other conditions.

In the Clauberg test the enzyme activity

of endometrium was elevated by progesterone in dose less than 2 mg with almost linear response, and consistent with its progestational proliferation.

If in the adult rabbit progesterone was given beyond five days, the enzyme activity reached the maximum, being lowered thereafter gradually to its beginning level, and did not always keep step with progestational proliferation of the endometrium.

Larger dose of estrogen inhibited the endometrial enzyme activity, while smaller dose accelerated it, as just its progestational proliferation.

During pseudopregnancy induced by gonadotrophin injection the maximum enzyme activity was reached around the eight days, and it corresponded to the life span of the corpus luteum. However, during gestation where progesterone production is kept in higher level until the late stage, there was also a upper limit of the enzyme activity around the eight day of pregnancy and it was presumed to have something to do with nidation of fertilized ovum.

The uterine muscle had no activity of the enzyme, but it revealed similar activity to the endometrium in the course of pregnancy.

Progesterone could not elevate the enzyme activity of the kidney, but that of the endometrium as above described. The hormonal action must be therefore indirect in the latter.

Diamox (a kind of inhibitor of carbonic anhydrase) could not affect the activity of the enzyme in the uterus distinctly as it did in the kidney.

13. On the Carbonic Anhydrase Activity of Uterus of the Rat

Kazuo ARAI

(Dept. Gynecology — K. Fujii)

The carbonic anhydrase activity of the rat's uterus was determined under some experimental conditions.

It was impossible to separate the endometrium from the myometrium in the rat's uterus, and the whole uterine tissue was utilized.

The enzyme activity of the uterus revealed

only a slight elevation following progesterone administration. It might be due to anti-substance against the enzyme included in the rat's serum.

Castration lowered the enzyme activity as long as two weeks. However, hypophysectomy did not influence it almost any way.

At the middle stage of pregnancy castration or treatment with estrogen, progesterone or their combination did not affect the enzyme activity, while hypophysectomy brought about distinctly elevated activity for unknown reason.

In the course of pregnancy the enzyme activity remained low at the early stage, but afterwards it was elevated until the eighteenth day and went down toward the delivery. It was postulated that the enzyme had anything to do with maintenance of

pregnancy in the rat. On the other hand, when decidualoma was experimentally induced only on the side of the uterine horn by progesterone treatment and traumatization, this horn was activer than the other having no decidualoma. This fact was not consistent with the lower activity at the early days of gestation, mentioned above.

Diamox lowered the enzyme activity of the uterus to some extent, but could not inhibit nidation as well as maintenance of pregnancy.

In addition, human endometrium was investigated concerning the menstrual cycle and gestation, and secretory endometrium was activer than proliferative one, and the activity of decidua was elevated in the first stage, being lowered gradually in the second stage of pregnancy.