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Abstracts of Original Articles

1. A Study of Pulmonary Function in Chronic Bronchitis

Naofumi TAKEUCHI
(2nd Dept. Internal Medicine– S. Obuchi)

The purpose of this study is to find out more accurately the obstructive ventilatory disturbances of chronic bronchitis.

For this purpose, I measured the airway resistances by the volume displacement bodyplethysmography and the total respiratory resistances by oscillation method for 26 patients of chronic bronchitis, who were diagnosed in accordance with Fletcher’s diagnostic criteria, 27 normal subjects and 7 patients of chronic pulmonary emphysema.

Moreover, I investigated the A-aDO2 of those patients and normal subjects to know the presence of gas exchange disturbance of chronic bronchitis.

1) The airway resistances which were measured by the panting method of the volume displacement bodyplethysmography have risen in all patients of chronic bronchitis. Of these patients, the subjects who showed normal pattern in spirometry have shown higher airway resistances and total respiratory resistances.

2) All patients of chronic bronchitis have shown the rising of A-aDO2, and were attended with slight or moderate hypoxemia with a few patients of severe hypoxemia.

3) In normal subjects, the airway resistances have not seen the effect of ageing. This result is agreed with the report which DuBois et al. measured by pressure type bodyplethysmography.

2. Physicochemical and Immunochemical Properties of Haptoglobin, Anthemoglobin Antibody and Their Complexes with Hemoglobin

Hajime TSUNOO
(Inst. of Medical Genetics– H. Nakajima)

The physicochemical and biochemical properties of hemoglobin associated with haptoglobin were compared with those of hemoglobin bound by specific antibody. The mechanism of enhanced peroxidase activity of hemoglobin bound by haptoglobin is concluded not to be the activation but the stabilization of hemoglobin at acidic pH by haptoglobin. Haptoglobin can protect the denaturation of hemoglobin by acid. Specific antibody, on the other hand, cannot enhance the peroxidase activity of hemoglobin, because it cannot protect acid denaturation of hemoglobin. Hemoglobin bound by antibody shows the higher affinity for oxygen than free hemoglobin, the biphasic Hill plot, and the slight preservation of heme-heme interaction and Bohr effect. These characteristic functions of hemoglobin bound by antibody show striking contrast to those of hemoglobin bound by haptoglobin.

From the differences mentioned above between hemoglobin-haptoglobin and hemoglobin-antibody complexes, it was suggested that histidine residues of hemoglobin might be masked by the complex formation with haptoglobin but not with antibody. Hemes of hemoglobin-antibody complex are not degraded by dithionite under aerobic condition whereas those of hemoglobin-haptoglobin complex are degraded, indicating that hemoglobin of hemoglobin-antibody complex is tetrameric whereas that of hemoglobin-haptoglobin complex is dimeric structure.

From the immunological studies, it was concluded that the antigenic groups of hemoglobin are not masked by the complex formation with haptoglobin and that binding sites...
of hemoglobin with haptoglobin and antibody are quite different. The important differences in the possible role in hemoglobin metabolism in vivo between haptoglobin and antibody were suggested.

3. Regional Distribution of γ-aminobutyric Acid in Cat Cord with Special Reference to the Physiological Function

Yuhei MIYATA
(Dept. Pharmacology—M. Otsuka)

A method was described for quantifying the GABA distribution in cat spinal cord at 200-500 μm resolution. Isolated spinal cord (L5-S1) was frozen and sectioned at about 150 μm thickness. The frozen tissue section was cut into 200 or 500 μm square blocks. The GABA content of each square tissue block was determined by enzymatic micromethods, and GABA distribution was mapped quantitatively. Average GABA concentrations were: 0.4 mmol/l in white matter, 1.2 mmol/l in ventral horn, and 1.7 mmol/l in dorsal horn. The highest concentrations of GABA (2-3 mmol/l) were found in the dorsolateral part of dorsal horn. The cauterization of blood vessels supplying the dorsal horn resulted in a marked diminution in (a) the size of dorsal root potential (b) the number of interneurons in the dorsolateral part of dorsal horn, and (c) GABA concentration in the dorsal horn. These results suggest that GABA is highly concentrated in the interneurons of dorsal horn and functions as a transmitter of presynaptic inhibition.

4. Actions of Substance P and Other Peptides on the Neurons of Frog Spinal Cord

Shiro KONISHI
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The effects of substance P and other peptides were studied on the neurons of isolated spinal cord of the frog. Substance P and certain related peptides, which have a common C-terminal sequence, -Phe-X-Gly-Leu-Met-NH₂ (where X=Ile, Tyr or Phe), exerted a remarkably strong excitant action on spinal motoneurons. On a molar basis, substance P was about 200 times, physalaemin 1500 times, and eleodein 2000 times more active than L-glutamate in depolarizing the spinal motoneuron in 0.4 mM Ca-Ringer's solution. Since the depolarizing action of substance P and related peptides persisted after the synaptic transmission was blocked by Ca-deficient (0-0.2 mM) Ringer's solution or by tetrodotoxin (10⁻⁶-10⁻⁷ g/ml), it was concluded that these peptides have a direct action on the motoneurons to induce the depolarization. Another group of peptides, bradykinin, angiotensin I and II, caused the depolarization of the spinal motoneurons by a transsynaptic mechanism. These peptides probably activated the interneurons and thus caused the release of the excitatory transmitter from the nerve terminals synapsing with motoneurons.

The possibility that substance P may be an excitatory transmitter of primary sensory neurons was discussed.

5. Studies on the Acute Cadmium-poisoning

I. Electron microscopic observations and elemental analysis of the mouse liver

Michiko KIMURA
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Acute Cadmium-poisoning of a mouse was induced by two intraperitoneal injections of 400 ppm Cadmium chloride solution. 2 hrs after the second injection, the mouse liver was cut into small blocks in the following chilled prefixative. The same volume of 8% paraformaldehyde and 1/7 M veronal acetate buffer solution was mixed and adjusted to pH 7.0, then Oxine was saturated in this fixative. Oxine makes insoluble precipitate with Cadmium (Cd) sensitively (0.125). Prefixation was proceeded by 2 hrs in ice. The blocks
were postfixed with 1% OsO₄, followed by dehydration and embedded in Epon. G-6-Pase (Gomori) and acid phosphatase (Karnovsky) were also examined. Hitachi HU-11E was used for ordinary observations and selected area electron diffraction, JEOS-100-B fitted with nuclear diode Silicon-detector for energy dispersive analysis of X-rays from an Epon embedded section (EDAX), and transmission type scanning electron image system (TSEI).

The cytoplasm was occupied by a large amount of smooth vesicles, instead of glycogen granules, granular endoplasmic reticulum (Ger) and Golgi apparatus disappeared. Some of the vesicles fused into each other, and made a big vesicle (Fig. 1). Mitochondria were surrounded with a kind of smooth vesicles. Vesicles included very small pieces of the cytoplasm, mitochondria and electron opaque fine precipitates. Those precipitates indicated the same electron diffraction pattern of Oxine-Cd precipitate (Figs. 9 & 10). This is considered that free Cd makes stable precipitate with Oxine in the fixative during the pre-fixation procedure. Electron opaque special granules (Sg) with limiting membrane were scattered in the cytoplasm (Figs. 1-10). Those Sg show somewhat crystalline nature and in the longitudinal section of a Sg fine striations could be seen along the long-axis, which estimated to be about 240 Å (Figs. 4, 5, 6, & 7).

The elemental composition of those Sg was detected by the aid of EDAX and TSEI system (Fig. 15). A thicker section was used for this purpose (2000 Å to 3000 Å). After the TSE-image had recorded (Figs. 15 & 16), the spot analysis for X-rays was tried. As shown in Fig. 15, the Sg were composed of the elements, such as sulfur, phosphorus, cadmium, and iron. Osmium, lead and uranium were also visible, as the section was treated with osmium, lead and uranium. Cd was also detected in the heterochromatin, nucleous (Fig. 16) and the fine precipitate of Oxine-Cd. The Sg should be occurred from the cell surface region of the Disc by the pinocytosis. Cd should be accumulated and become non-toxic substance combining with proteins, which contain much sulfur, such as lysine. G-6-Pase was observed in the remaining Ger (Fig. 18-A), but irregular distribution was observed in the vesicular cytoplasm (Fig. 18-B). Acid phosphatase was located in the Sg (Fig. 17, A & B, arrows & Sg).

6. Interaction of the Cartilage Insoluble Collagen Fraction with Chondroitin Sulfate C

Eisuke HANADA

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The insoluble collaglass fraction (ICF) was isolated from bovine nasal cartilage by exhaustive extraction by aid of homogenization with 8 M urea-1 M NaCl. The amino acid composition of ICF was essentially similar to that of soluble collagen ever reported, except that the values of glycine and hydroxypoline were only slightly lower than those of soluble collagen, respectively. The ICF also contained unremovably carbohydrate species (8% as a whole) such as hexose, hexosamine, uronic acid, and sialic acid.

Chondroitin sulfate C (ChS-C) was bound to ICF (50 Î¼g/mg) at pH 3.4 (0.01 M Na citrate buffer), but slightly at pH 7.0 (0.01 M Na citrate buffer) (Î¼g/mg). When a small dose of ChS-C was bound at pH 3.4 to an ICF column, ChS-C was not eluted by pH gradient elution from pH 3.4 to 7.0, but it was eluted at pH 7.0 with NaCl gradient from 0 to 1 M. The ChS-C saturated ICF column released ChS-C with pH gradient as well as NaCl gradient elution at pH 7.0. The modified ICFs prepared by reacting with acetic anhydride, glyoxal or carbodiimide exhibited characteristic elution patterns of various biopolymers (ChS-C, Schubert's PPL (proteoglycan)), albumin, Ï²-globulin, RNA, and cytochrome c). Since the distribution of dissociable (polar) amino acid residues on collagen polypeptide chain was uneven, three (basic, neutral, and acidic) regions are presumed to participate in the pH-dependent adsorption to ICF and elution from ICF of those biopolymers, where the pH-dependent dissociation of the polar groups of those biopolymers
is mutually responsible for the respective elution patterns.

7. On the Change in Acid Mucopolysaccharide of Dog Carotid Artery after Unilateral Ligation II. Correlation of acid mucopolysaccharides with collagen and carbohydrate components of estimated glycoprotein fraction

Shinji KAJIGAI
(Inst. for Cardiovascular Diseases—K. Anan)

The dog carotic common artery was unilaterally (right side) ligated at two positions of a few centimeter distance. The content of connective tissue components of arterial wall of the inter-ligation zone was estimated by measuring uronic acid, glucosamine, galactosamine, hexose, and sialic acid. The difference between the content of total hexosamine and uronic acid was used as a measure for the relative amount of glycoprotein (GP)-carbohydrate moiety. Hydroxyproline and proline were determined to estimate the content of collagenous protein(s). The ligation tended to increase GP and acid mucopolysaccharide (AMPS), especially chondroitin sulfate C, with which the hydroxyproline content was negatively correlated. It is implied that the ligation up to 4 weeks gives a rise to GP and AMPS presumably as a pre-stage of fibrillation reaction (collagen enrichment) though there was observed a macroscopic sclerotic change of the ligated arterial wall.

8. A Histopathological Study of Paget's Disease of the Breast

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Paget's disease of the breast was described in detail and its histogenesis was discussed. Thirty-two cases with histologically proven Paget's disease of the breast were seen at Tokyo Medical and Dental University Hospital and Cancer Institute Hospital, Tokyo, between 1946 and 1971. This comprised 1.3% of all breast cancers seen during this interval.

In conclusion, Paget's disease can be divided into two categories; Paget's carcinoma and Pagetoid carcinoma. Intraepidermally spreading in situ carcinoma originating from the mammary duct belongs to Paget's carcinoma; infiltrating carcinoma of common type partly with intraepidermal extension, to Pagetoid carcinoma. Histogenesis of these appears to be different. According to this classification, the thirty-two cases of Paget's disease were divided into 14 cases of Paget's carcinoma and 18 cases of Pagetoid carcinoma. The average age of Paget's carcinoma patients was 55.6; that of Pagetoid carcinoma, 50.9.

Periductal lymphoid cell infiltration was characteristic of Paget's carcinoma.

In Paget's carcinoma, extension of Paget's cells in the squamous epithelium of the nipple was 3.6 mm on an average per year.

Electron microscopy revealed that Paget's cells of both Paget's and Pagetoid carcinomas provided every feature of ductogenic carcinoma.

9. Surgical Treatment of Pancreaticoduodenal Artery Aneurysms

Ryoji HATANO, Toshitada HATANO, Tohru SAKAMOTO, Toshio TSUKUURA, Taisei MAEMURA, Hiroshi NAGAOKA, Takashi YAMADA and Tadashi MURAKAMI
(1st Dept. Surgery—T. Murakami)
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Two aneurysms (1.5×1.5 cm & 3.5×3.5 cm) of arteriosclerotic origin arising from pancreaticoduodenal artery were successfully resected from a 48 year-old female. The aneurysms were first suspected by radiographic demonstration of a round calcification in the right upper quadrant of the abdomen, and were confirmed by a selective superior mesenteric arteriography. Both aneurysms were located at the head of the pancreas.
Postoperative course was complicated by leakage and accumulation of pancreatic juice from the bed of aneurysms. Following the drainage procedure, a large doses of antitrypsin, GCP-choline, antibiotics, anticholinergics, and steroid were administered with an IV hyperalimentation, and the patient was recovered from the complication. Postoperative angiogram revealed a near total occlusion of the arterial anastomosis with a development of collaterals, however there is no evidence suggestive of ischemia of the viscera. Major branches of celiac artery was perfused via posterior arcade of pancreaticoduodenal artery.

Aneurysm of the pancreaticoduodenal artery is a rare lesion, and a preoperative correct diagnosis is usually difficult. At present, 19 cases have been reported in the world literatures. There has been no report of this lesion in this country, the present case being the first report of a case. Since this particular aneurysm is easy to rupture, surgical excision is warranted in case the presence of the aneurysm is confirmed. Although postoperative complication due to leakage and accumulation of pancreatic juice is rather unique with this lesion, prognosis will usually be fair, if an aggressive treatment is promptly instituted.

10. Naturally Occurring Agglutinins against Bacterial Fimbriae

Toyoko HIKAWA

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It has frequently been observed that Shigella diagnostic antisera agglutinate nonspecifically some strains of Shigella or of completely different species of the Enterobacteriaceae. Since fimbriae were suggested to be involved in such aberrant agglutination reactions, we have investigated the reaction of fimbriated shigellae against antifimbrial agglutinins.

Shigella strains used were 3 fimbriated and 3 nonfimbriated cultures. Sera tested consisted of 4 Shigella diagnostic grouping antisera, 6 type-specific and 3 group-specific antisera for Shigella flexneri, as well as Salmonella diagnostic antisera and normal rabbit sera. To detect the presence of antifimbrial agglutinins, slide agglutination, tube agglutination and complement fixation tests were carried out. Agglutinin absorption tests were also performed with Shigella diagnostic antisera.

With fimbriated shigellae, the diagnostic antisera produced marked nonspecific agglutination reactions. Employment of heat-killed suspensions of the fimbriated strains or a nonfimbriated variant eliminated such aberrant reactions completely. The nonspecific agglutinations also disappeared when the antiserum was absorbed by fimbriated bacteria, but did not disappeared when absorbed by nonfimbriated ones. In complement fixation reactions of diagnostic rabbit antisera with a purified fimbrial preparation as antigen, antifimbrial antibodies were demonstrated. Pursuit of the origin of antifimbrial agglutinins revealed that normal rabbit sera contained such agglutinins.