

ABSTRACTS

1. STUDIES ON THE INFLUENCE OF ANTITUBERCULOUS AGENTS UPON TISSUE RESPIRATION

PART 3. INFLUENCE OF PZA ON TISSUE RESPIRATION OF MICE

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The following 3 groups of mice were subjected to the experiments to investigate the influence of PZA upon tissue (liver, spleen and lung) respiration.

Group A. Mice infected with human tubercle bacilli "H₃₇R_v" and treated with PZA

Group B. Mice infected with human tubercle bacilli "H₃₇R_v," untreated

Group C. Normal mice

The results obtained were as follows :

1) In hepatic tissue respiration, no difference was observed between the three groups. On the other hand, in the amount of splenic and pulmonary tissue respiration, group A and B were observed to have no difference between them, but each was found to be above group C.

2) Generally speaking, the tissue respiration of the three groups was suppressed by PZA added to the medium in a high concentration (1-10 mg/ml), except the hepatic in group C and the splenic in groups A and B, which suffered no change. A low concentration (0.1 γ /ml) produced no change in the tissue respiration except the hepatic and the pulmonary in group A, which were accelerated.

2. IMMUNOLOGICAL STUDIES IN TUBERCULOSIS

PART 18. ELECTROPHORETICAL STUDIES ON SERUM IN TUBERCULOSIS No. 1. OBSERVATION ON PATIENTS WITH PULMONARY TUBERCULOSIS

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Experiments were made for the purpose of clarifying the relation between the electrophoretical pattern of the serum protein and the progress of tuberculosis, and between the γ -globulin content of serum and the intensity of tuberculin allergy and the antiserum titer measured by Middlebrook-Dubos test.

The subjects involved in the present study were 64 patients with pulmonary tubercu-

losis and 15 healthy tuberculin-positive persons.

The results obtained are summarized as follows :

1) No marked difference in the total protein content was observed between the patients and the healthy subjects, but in the former the albumin content was observed to be smaller, and all the globulins, particularly γ -globulin, larger than in the latter.

2) Increase of the γ -globulin content was observed to run parallel with aggravation of clinical symptoms.

3) The erythrocyte sedimentation rate was found to have close correlation with the γ -globulin content.

4) No parallel correlation was found to exist between the intensity of tuberculin allergy and the γ -globulin content.

5) By applying the absorption test it was found that the antibody responsible for Middlebrook-Dubos reaction was contained mostly in the γ -globulin fraction. However, parallel relation was not always observed between the γ -globulin content and the antibody titer. Thus the γ -globulin produced in the serum by tuberculous infection seems to consist of a fraction which is a specific antibody and another which is not.

3. IMMUNOLOGICAL STUDIES IN TUBERCULOSIS

PART 18. ELECTROPHORETICAL STUDIES ON SERUM IN TUBERCULOSIS

No. 2. OBSERVATION ON RABBITS

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The following 3 groups of rabbits were employed in the present study.

Group A. Four rabbits infected with human tubercle bacilli "H₃₇R_v"

Group B. Four rabbits inoculated with heat-killed human tubercle bacilli "H₃₇R_v"

Group C. Five rabbits injected, five times at 3-day intervals, with the recipient's own red cells sensitized with OT.

Electrophoretical studies and Middlebrook-Dubos reaction tests were carried out on the sera of groups A and B weekly after the treatment and of group C after each injection. When the antibody titer reached a maximum, the antibody was absorbed in group A and B with the bacilli and in group C with OT-sensitized red cells, or the bacilli, and the relation between the electrophoretical pattern and the antibody titer was observed.

The serum of group C, moreover, was fractionated with ammonium sulfate, and each fraction was tested for the agglutinating activity against OT-sensitized erythrocytes.

The results obtained are as follows :

1) In the sera of groups A and B, rise of the antibody titer was observed to accompany a change of electrophoretical pattern of the serum protein . . . slight increase of total protein content consisting of marked increase of γ -globulin, slight increase of α - and β -globulin and decrease of albumin.

2) In the serum of group C, increase of γ -globulin was observed to be small despite the marked rise of the antibody titer.

3) By absorption with heat-killed human tubercle bacilli "H₃₇R_v," the sera of the 3 groups showed decrease of γ -globulin and loss of antibody.

In the serum of group C, decrease of γ -globulin by absorption was less than in the sera of groups A and B, and ran parallel with the increase due to immunization.

Moreover, in the serum of group C, γ -globulin was decreased to the same extent by absorption with the bacilli and with OT-sensitized red cells.

4) Among the protein fractions of the serum of group C, only the γ -globulin fraction showed agglutinating activity for OT-sensitized red cells.

5) From the data presented, it was revealed that the antibody was mostly in the γ -globulin fraction of the antiserum, but accounted only for a part of the increase of the fraction.

4. STUDIES ON ANAMNESTIC SERUM REACTION IN EGG-ALBUMIN IMMUNIZATION

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Egg-albumin was injected to a number of rabbits to produce the specific antibody in their blood stream. When, after some time, the amount of the antibody had decreased the animals were given injections of the same antigen or typhoid vaccine or irradiated with x-rays, and the anamnestic reactions . . . albumin sensitized erythrocyte agglutination, complement fixation and precipitation reaction . . . of their sera were observed.

Furthermore, the anamnestic antibodies were compared quantitatively and qualitatively by means of Ouchterlony's method with the antibodies produced by the primary immunization.

In addition, the difference of antigenicity between crude and purified egg-albumin was examined.

The results obtained are summarized as follows :

1) Needless to say, the antigen used in the primary immunization was found to be effective in producing all the antibodies tested for. X-ray irradiation was seen to

produce agglutinin against the antigen-sensitized red cells and complement-fixing antibody while typhoid vaccine produced the former only.

2) When booster injection of egg-albumin was carried out, the latent period for antibody production as well as the time required for the antibody titer to reach a given high level was found to be much shorter than was the case after the first immunization. When x-rays or typhoid vaccine was used there was no reduction of the latent period and the antibody titer was low.

3) By the method of double diffusion in agar, the sera of rabbits injected with egg-albumin and the antigen were observed to produce a varying number of precipitation bands, as shown in the following table.

injected antigen	IE		PE	
antigen in test	IE	PE	IE	PE
Antibody				
in primary immunization	9	5	1	0
in secondary immunization	9	5	8	5

IE: impure egg-albumin

PE: purified egg-albumin

From the data presented, it may be concluded that IE has one more antigenic determinant and is stronger in antigenicity than PE. Therefore, in this line of work with PE, the intensity of primary immunization must be taken into consideration.

5. STUDIES ON THE RESISTANCE OF MICROORGANISMS TO VARIOUS CHEMICALS

PART 10. STUDIES ON THE DOUBLY DRUG-RESISTANT TUBERCLE BACILLI
No. 3. PRODUCTION OF TUBERCULIN BY DOUBLY DRUG-RESISTANT STRAINS

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In the previous experiments, singly and doubly drug-resistant tubercle bacilli were isolated after successive culture of the SM-resistant and INAH-resistant strains and their parent (susceptible) strain "H₂" on 1% Ogawa's solid medium containing anti-tuberculous agents such as SM, PAS, Tbl, INAH, IHMS, VM and o-aminophenol (OM).

In the present study, the three original strains and the isolated strains were cultivated in Sauton's medium under conditions as nearly identical as possible. After 8 weeks' cultivation OT was prepared from each of the culture filtrates by the conventional method.

The OT thus prepared from the isolated strains were compared with the OT from the original drug-sensitive strain about their potency in producing skin reaction on tuberculous patients.

1) The SM-resistant strain was found to produce OT of almost equal potency as the OT from the parent strain and the INAH-resistant strain to produce OT of somewhat higher potency.

2) The INAH-SM-resistant strain derived from the SM-resistant strain and that derived from the INAH-resistant one did not differ from each other in the potency of their OT, which were almost equal in potency to the OT from the SM-resistant strain.

3) The OT from the strain which had developed VM-resistance was found to be a little less potent than the OT from the original strain.

4) The INAH-resistant strain and the IHMS-resistant strain were found to yield OT of equal potency; the same was the case with the SM-INAH-resistant strain and SM-IHMS-resistant strain.

5) The three original strains developed PAS or Tbl resistance without any change in the potency of their OT.

6. STUDIES ON THE RESISTANCE OF MICROORGANISMS TO VARIOUS CHEMICALS

PART 12. CHANGE OF SM- AND INAH-SENSITIVITY IN AVIAN TUBERCLE BACILLI BY CONTINUOUS IRRADIATION WITH P³²

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Using the drug-sensitive avian tubercle bacillus "Takeo strain," and the SM- and INAH-resistant strains isolated from it, the following five series of experiments were carried out in vitro to investigate the influence, upon the drug-sensitivity of the three strains, of continuous irradiation with P³² in successive culture media, in the presence of antituberculous agents or otherwise.

- I. Exposure of the three strains to P³²
- II. Exposure of the sensitive strain to SM and P³²
- III. Exposure of the sensitive strain to INAH and P³²
- IV. Exposure of the sensitive strain to SM
- V. Exposure of the sensitive strain to INAH

The results obtained were as follows:

- 1) No change was observed in the drug-sensitivity or growth of any of the three strains by continuous irradiation with P³² when the dosage was 1-100 μ c/ml.

2) In Experiment II, bacilli with higher SM-resistance appeared in the earlier stages of the exposure than in Experiment IV, while no significant difference was observed in the development of INAH resistance between Experiments III and V.

7. ULTRASTRUCTURE OF THE PULMONARY ALVEOLUS

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The Ultrastructure of pulmonary alveoli was studied by the electron microscope on surgically excised pieces of human lung tissue. The results obtained are as follow:

1) The alveolar wall is covered with a thin continuous epithelial lining which may be regarded as an extension of epithel-cell with nuclei. There is an electron dense basal membrane beneath the epithelium.

2) The wall of pulmonary capillaries is covered with endothel-cells with nuclei which carry a basal membrane, being similar to the one of alveolar wall.

3) There is septal stroma between the pulmonary capillary and the alveolus.

4) No significant difference is seen about the microstructure of alveolus and capillary between the lung tissue of hilar region and that of peripheral area of the lung.

8. ELECTROCARDIOGRAPHIC CHANGES SUBSEQUENT TO RESECTIONAL SURGERY OF PULMONARY TUBERCULOSIS

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The authors have compared electrocardiographic findings examined to 4 months after resectional surgery of the lung with those before the operation. Changes were seen after operation in 43 cases (69 per cent) out of 62, and were generally most conspicuous in the first month, gradually diminishing later stage more than 3 months.

Most findings seen after operation showed cardiac rotation, cardiac transposition, change of P-, ST-, and T-waves, and inclination of transitional zone. Cardiac rotation was the most frequent of all the findings.

There was no particular difference in electrocardiographic changes according to the operative technique, operated side, or the degree of inflation of the residual lung tissue. However, the cardiac rotation remained for comparatively longer periods in the case of right side lobectomy.

After operation, P-, ST-, and T-fluctuations were changed both toward their improvement by operative treatment and toward their aggravation by operative intervention. Eventually, they became to show almost normal in pattern in the postoperative course more than 3 months or so.

Inclination of transitional zone was very often observed in the case of extensive surgery over lobectomy and it was apt to incline toward the operated side.

9. SIGNIFICANCE OF BRONCHIAL LESIONS IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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Bronchial lesions have been observed by bronchoscopic examination on 100 cases of pulmonary tuberculosis and they were taken into consideration together with roentgenologic findings of the lung, bacillary findings of the sputum, method of administered chemotherapy, and pathological findings of the resected specimens. The results obtained were as follows;

1) Bronchial lesions were seen by bronchoscopy in 31 per cent of the 100 cases, 22 per cent in cavitory lesions and 9 per cent in non-cavitory.

2) Bronchial lesions were observed much more severely, according to order of giant cavity, destroyed lung, caseous lesions, coin lesion and residual cavity of thoracoplasty. Bronchial lesions were more frequently found in the cases of A-, B- and F-type of Gakuken's classification of pulmonary tuberculosis.

3) The sputum was positive for tubercle bacilli in 83 per cent and negative in 17 per cent, out of the 31 cases where bronchial lesions were definitely seen by bronchoscopy. The severity of bronchial lesions and Gaffky number of tubercle bacilli ran almost parallel to each other.

4) Bronchial lesions were found by bronchoscopy most frequently in the cases where only a short period of chemotherapy was given before the examination.

5) Pathological examination of resected specimens revealed that the bronchi were actually much more involved with lesion in those cases where bronchoscopy showed inflammatory changes and the sputum was positive for tubercle bacilli.

However, bronchial lesions could sometimes be pathohistologically recognized in

resected specimens even in the cases where bronchoscopic findings were negative.

6) There occurred four bronchial fistulae after resectional surgery of the lung among the cases where bronchial lesions were seen by bronchoscopy before the operation. These cases were also assumed to contain the resistant tubercle bacilli against the drugs which were regarded as a cause of the fistula.

10. APPLICATION OF NAPHTHIONIN IN RESECTIONAL SURGERY OF THE LUNG

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The chemical compound, Naphthionin was taken into examination as a hemostatic both by experimental study and by clinical application. The following results were obtained :

1) Intramuscular administration of Naphthionin brought a rapid and positive hemostatic effect—shortening of bleeding- and coagulation-time—which began to appear 1 hour after administration, reached the maximum in another hour and remained as long as 6 hours.

2) Naphthionin was applied for the purpose of hemostasis to 40 cases of resectional surgery of pulmonary tuberculosis. Considerable decrease of bleeding was obtained during operation of lobectomy cases in the presence of dense pleural adhesion and of segmental resection.

3) No marked side effect of Naphthionin was observed.

11. INHIBITION OF STREPTOLYSIN S BY TUBERCLE BACILLI

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It was found that, when suspended in saline, the organisms of certain strains of Mycobacteria, including human and bovine tubercle bacilli, release a substance which is capable of inhibiting the hemolytic action of streptolysin S. On the other hand,

M. avium, *M. phlei*, *M. tuberculosis* 607. and a chromogenic acid-fast bacillus 'Ishii' were found to have no such inhibitory activity against streptolysin S.

The anti-lytic activity of tubercle bacilli greatly varies with strains; the organisms of such human strains as H₂, Frankfurt, and H₃₇R_a exhibited a well-marked inhibiting action on streptolysin S, while those of H₃₇R_v, Kawakami, and Aoyama B, and two bovine strains, No. 10 and BCG, all were found to have far weaker anti-lytic effect on streptolysin S.

The age of culture and the kind of culture medium did not affect the anti-streptolysin S property of the organisms.

The organisms of streptomycin-resistant variants of tubercle bacilli did not differ in the anti-lytic activity from those of the original streptomycin-sensitive strains.

The anti-streptolysin S substance from tubercle bacilli was found to be non-dialysable, destroyed by heating at 100°C for 30 minutes, and readily inactivated by pepsin, though quite resistant to the action of trypsin, papain, lipase and amylase.

Among a variety of bacteria other than tubercle bacilli, it was demonstrated that both *B. subtilis* and *B. mesentericus* are able to exert a similar inhibition of streptolysin S.

12. INFLUENCE OF TREATMENT OF ERYTHROCYTES WITH TANNIC ACID UPON THEIR SUSCEPTIBILITY TO STREPTOLYSIN S

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In the present study it was demonstrated that treatment of erythrocytes with tannic acid (1: 2,000-50,000) brings about a change in the properties of the cells, rendering them more or less unsusceptible to the hemolytic action of streptolysin.

The streptolysin S used was the purified sample (minimum hemolytic concentration, 1:20 mill), prepared from 1% nucleic acid-broth culture of hemolytic streptococci.

Erythrocytes of humans, cattle, sheep, goats, dogs, guinea pigs and rabbits were used, but the majority of experiments were made with guinea pig erythrocytes. The red cells were washed in phosphate-buffered saline (pH 7.3) and suspended in two volumes of the saline. The treatment of erythrocytes with tannic acid was carried out as follows: 4 ml of a solution of tannic acid in buffered saline and 0.4 ml of erythrocytes were mixed and kept under specified conditions. The red cells were then centrifuged, washed and resuspended in 20 ml of buffered saline.

The hemolytic titration was made by the method routinely used in our laboratory. The effect of tannic acid treatment of erythrocytes on their susceptibility to strepto-

lysin S was studied by examining the hemolytic action of streptolysin S on treated and untreated (control) red cells.

Erythrocytes of guinea pigs, when treated with a solution (1: 2,000-5,000) of tannic acid at 5°C for ten minutes, were completely resistant to the hemolytic action of streptolysin S in a concentration as high as 1: 500,000.

Tannic acid was most effective in reducing the susceptibility of erythrocytes to streptolysin S, when it was used in the neutral or slightly alkaline medium and at low temperatures.

Erythrocytes of various animals differed markedly in the behaviour to the action of tannic acid. Erythrocytes of cattle and sheep were most strongly affected, followed by red cells of goats, guinea pigs, humans and dogs, in that order, while the susceptibility of rabbit cells was not affected at all by tannic acid.

Publications not appearing in the Ann. Rep. Tbc.

Kanazawa (1958)

- 1) **Mukozka, K.:** Studies on the Influence of Nitrous Acid upon the Immunogenic Properties of Tubercle Bacilli. Part 2. Comparative Study of the Vaccinating Properties of Nitrous Acid-killed BCG and Living BCG Vaccines in Guinea Pigs. *Japan. J. Tuberc.*, 5 (3-4), 101, 1957.

Vaccines were prepared from young culture of BCG grown on Sauton's medium and rendered nonviable by treatment with nitrous acid for various length of time at ice-cold temperature in acetate buffer medium (pH 4.1-4.2).

Comparison was made on guinea pigs of the immunizing activity of HNO₂-killed BCG, living BCG, and the heat-killed BCG, the HNO₂-killed vaccine of the virulent human strain H₂ being used as the comparison vaccine. Animals of all the groups vaccinated intraperitoneally with the HNO₂-killed BCG developed a marked degree of immunity comparable to that induced by the vaccination with living BCG against tuberculous infection with the virulent human strain H₂. In contrast to this, there was no specific immunity in the group vaccinated with the heat killed BCG.

- 2) **Uragami, N.:** On the Tuberculin-Inactivating Effect of Bromine. *Japan. J. Tuberc.*, 6 (1), 1, 1958.

It was shown that bromine, under suitable conditions, readily inactivated the specific biological activity of tuberculin, including Old Tuberculin, purified citrate-tuberculin, and o-aminophenol azo-tuberculin.

The rate of bromine inactivation of tuberculin depended largely upon temperature and concentration of bromine. Within the certain limit of temperature bromine rapidly inactivated tuberculin, whereas at a higher temperature the rate of inactivation decreased even in the presence of excess of bromine.

The variation of pH did not seriously affect the outcome of the bromine effect.

The bromine inactivation of tuberculin was more or less completely reversed by the presence of other nonspecific proteins, and simple biogenic substances such a svarious amino acids, unsaturated fatty acids, and uracil.

- 3) **Funasaki, Y.:** Fundamental Studies in Chemotherapy of Tuberculosis. Part 68. On the Drug-Susceptibility of a Chromogenic Acid-Fast Bacillus from Human Source, with Special Reference to the Effect of o-Aminophenol and its Derivatives. *Japan. J. Tuberc.*, 6 (2), 51, 1958.

A number of substances, including various antituberculous and antimicrobial agents with special reference to o-aminophenol and its derivatives, were screened for *in vitro* bacteriostatic activity against an atypical chromogenic acid-fast bacillus, the Ishii strain, isolated from a patient with roentgenographic findings

simulating tuberculosis.

It was shown that o-aminophenol and certain of the phenoxazone derivatives, i.e., 3-chloroacetyl-amino-phenoxazone-(2) and 3-(N, N-diethylglycylamino)-phenoxazone-(2), exhibited potent growth-inhibitory activity against this strain, while the other antituberculous agents such as streptomycin, p-aminosalicylic acid and isoniazid, and various antimicrobial drugs were all either far less effective or without effect.

Among other substances examined, two phenazine derivatives, amethyst violet and indamine blue, showed likewise a strong inhibition of the growth of the organism.

- 4) **Saito, T., Konishi, K., Matsuda, T., Masuya, H. and Hodatsu, H. :** Use of Cr⁵¹-labeling Method for Immunological Studies.

Part 1. Difference in the Post-injection Survival of the Recipient's own Cr⁵¹-labeled OT-sensitized Red Cells between Normal and Immunized Rabbits. *Japan. J. Tuberc.*, 6 (2), 47, 1958.

The experiments were carried out of measuring, by the Cr⁵¹-labeling method, the rate of disappearance of the injected OT-sensitized red cells of the recipient's own from the circulation of the animal. The results of a far higher disappearance rate of OT-sensitized red cells from the circulation of the immunized animals with the sensitized red cells seem to constitute strong evidence for the antigenicity of their OT-sensitized red cells, particularly when considered together with the fact that both the hemagglutination and hemolysis tests carried out with the serum obtained from the immunized animal did give a positive reaction.

- 5) **Kakishita, M., Sugibayashi, A., Ueda, M., Nishimura H. and Yokoi, K. :** Curative Effect of Achromycin-V upon Paratyphoid A. *Achromycin-V-bunkenshu*, No. 4, 4, 1958.

No difference was observed in the curative effect on paratyphoid A between chloromycetin and achromycin-V.

- 6) **Yoshida, K., Nakaguchi, A., Yamamoto, S. and Nakase, S. :** Tuberculin Skin Reaction after BCG-inoculation. *J. Japan. Med. Associ.*, 36 (6), 394, 1958.

Men who acquired strong tuberculin skin allergy after BCG-inoculation showed same skin sensitivity to both o-aminophenol azo-tuberculin (0.05 γ /0.1ml) and OT (1/2,000 0.1ml) for a certain period of time. Thus in that period, differentiation of BCG-inoculation from natural infection is impossible by means of simultaneous use of the two tuberculins.

- 7) **Koshimura, S., Shimizu, R., Masusaki, T., Ohta, T. and Kish, G. :** On the Formation of Streptolysin S by Hemolytic Streptococci Acting on Tumor Cells. *Japan. J. Microb.*, 2, 23, 1958.

Okamoto showed in 1939 that streptolysin S production in vitro is markedly

enhanced by the addition of yeast ribonucleic acid to the medium. In the course of extending the study on the nucleic acid effect it was recently observed in our laboratories that the contact of tumor cells with living washed hemolytic streptococci in vitro caused the production of a significant quantity of streptolysin S.

Attention should here be directed to the following points:

1) The supernatant of the resting cell mixture of Ehrlich carcinoma cells and living hemolytic streptococci was effective in causing hemolysis up to a dilution of 1:32.

2) No detectable hemolysin was formed either in the suspension of the carcinoma cells alone or in the suspension of living hemolytic streptococci alone.

Quite similar results were also obtained in the experiment, in which Yoshida sarcoma cells were employed in lieu of Ehrlich carcinoma cells.

- 8) **Koshimura, S., Nakanaga, K., Kon-i, C., Daimon, H. and Shimizu, R. :** Experiment on the Formation of Streptolysin S by Hemolytic Streptococci Acting on Leucocytes. *Juzen-igakkai-zasshi*, 60, 1437, 1958.

In the paper are presented to show that when living hemolytic streptococci are made to act in vitro on leucocytes of guinea-pig an appreciable amount of streptolysin S is produced. It seems reasonable to say that the lysin is produced, as in the case of experiment with tumor cells and living hemolytic streptococci, at the expense of RNA contained in leucocytes.

- 9) **Masusaki, T. :** Experimental Anticancer Studies. Part 7. On the Influence of 6-(2'-Hydroxy-3', 5'-dibromophenylazo)-4-n-hexylresorcinol Analogues and Various Anti-cancer Agents upon Ehrlich Carcinoma Cells in the in Vitro-in Vivo Test Experiment. *Juzen-igakkai-zasshi*, 60, 1512, 1958.

It has been shown in 1956 by Koshimura and Hirata et al. that (1) 6-(2'-hydroxy-3', 5'-dibromophenylazo)-4-n-hexylresorcinol (Azo-36), when administered intraperitoneally to rats bearing Yoshida sarcoma, caused destruction of the tumor cells and prolongation of life of the experimental animals, and that (2) the compound, when given intraperitoneally to mice, to which Ehrlich carcinoma cells were inoculated intraperitoneally, was also effective in restraining the tumor growth.

The present paper describes the data obtained in the experiments, in which ten of Azo-36 homologues and five of commercially available anti-cancer agents, i. e., nitromin, azan, 6-mercaptapurine, sarkomycin and urethane, were studied for their influence upon Ehrlich carcinoma cells by employing the in vitro-in vivo test method.

The conditions of the in vitro-in vivo test system was as follows: 1) immersion of the carcinoma cells in phosphate-buffered solution of a drug should be tested at 37°C for 2 hours; 2) injection of the suspending mixture thus obtained should be made into the peritoneal cavity of a mouse (ca. 6 mill. carcinoma cells/mouse).

Results :

I) Of ten hydroxyazobenzene derivatives, following seven compounds were tested to give a positive result. Among them Azo-36 was found to be most effective in prolonging the life of the experimental animals.

- 1) Bis (2'-hydroxy-3', 5'-dibromophenylazo)-L-tyrosine (Azo-8)
- 2) 6-(2'-Hydroxy-3',5'-dibromophenylazo)-4-n-hexylresorcinol (Azo-36)
- 3) 6-(2'-Hydroxy-5'-carboxyphenylazo)-4-n-hexylresorcinol (Azo-51)
- 4) 6-(2'-Hydroxy-5'-methylphenylazo)-4-n-hexylresorcinol (Azo-74)
- 5) 6-(2'-Hydroxy-3',5'-dichlorophenylazo)-4-ethylresorcinol (Azo-84)
- 6) 6-(4',6'-Dibromo-2'-carboxyphenylazo)-4-n-hexylresorcinol (Azo-96)
- 7) 6-(2'-Hydroxy-3',5'-dibromophenylazo)-4-carboxyethylresorcinol (Azo-98)

II) Under the experimental conditions stated above, nitromin was tested to prove to be somewhat more effective than Azo-36, and sarkomycin was found to be much less effective. But, experiment carried out with azan, 6-mercapto-purine and urethane gave all negative results.

- 10) **Okamoto, H., Koshimura, S., Hirata, R., Murasawa, K., Bando, Y. and Shimizu, R. :** Some Data in Anti-cancer Experiments. *Z. Krebsforsch.*, **62**, 408, 1958.

Die Bildung von Streptolysin-S durch den Streptococcus haemolyticus wird durch Zugabe von Nucleinsäure gesteigert. Die hemmende Wirkung von hämolysierenden Streptokokken auf Ehrlich-Ascitescarcinom und Yoshida-Ascitesarkom ist dadurch zu erklären, dass die Keime auf Kosten der in Tumorzellen enthaltenen Ribonucleinsäure Streptolysin bilden. Anderen Keimen fehlt diese Eigenschaft. Auf einschlägige Beobachtungen an Menschen wird hingewiesen.

Da chemische Stoffe, welche die Hämolysin-S-Bildung durch Streptokokken vermindern oder gar aufheben, dies dadurch tun, dass sie in den auch für das Wachstum der Tumorzellen wichtigen Ribonucleinsäure-Stoffwechsel eingreifen, wurde unter derartigen Stoffen nach anticancerös wirkenden Mitteln gesucht und ein sehr wirksames (Azo 106) gefunden.

- 11) **Murasawa, K. and Altmann, V. :** Primary Lung Cancer in Pulmonary Tuberculosis (A Study Based on 570 Postmortem Examinations) *Sea View Hospital Bulletin*. **62**, 37, July, 1958.

1. In 570 consecutive autopsies performed during a ten year period in a tuberculosis hospital there were 39 cases of primary lung carcinoma.

2. There was close anatomical association between active pulmonary tuberculosis and primary lung carcinoma in fourteen instances corresponding to about 2.4 per cent of all cases. This figure corresponds to the one expressing the probability of developing cancer of lung among a comparable average population.

3. No etiological relationship was detected between lung tuberculosis and carcinoma.

4. If there is any increase in the frequency of cases with lung cancer in tuberculosis hospitals, the reasons are other than a direct causal relationship between the two conditions.