



Title	Abstracts of “ Tuberculosis Research ” Vol. 23/24, 1966
Citation	結核の研究, 23-24, 79-82
Issue Date	1966-3-25
Doc URL	<a href="http://hdl.handle.net/2115/26770">http://hdl.handle.net/2115/26770</a>
Type	bulletin (article)
File Information	23_24_P79-82.pdf



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## Abstracts of " Tuberculosis Research "

Vol. 23/23, 1966

Effets des drogues dites antiallergiques et anti-inflammatoires et des antimétabolites sur le développement de l'allergie tuberculique expérimentale.

Kazuo MAEDA

Afin d'élucider le mécanisme de l'allergie tuberculique, nous avons entrepris une série d'expériences, dans lesquelles nous avons cherché, en utilisant des cobayes et des lapins, des drogues qui exerceraient une influence inhibitoire sur l'allergie tuberculique. Les drogues testées étaient : glycirrhizine, oxyphenbutazone, éthylène-diamine-tétra-acétate de disodium (EDTA), acidomycine, 8-azaguanine, améthoptérine, aminoptérine et 6-mercaptopurine (6-MP). Les doses, les routes et les débuts de l'administration des drogues étaient différents selon les expériences.

Voici les résultats :

- 1) Chez des cobayes, la glycirrhizine, l'oxyphenbutazone, l'EDTA, l'acidomycine n'ont exercé aucune influence inhibitoire sur le développement de l'allergie tuberculique, quand leurs administrations quotidiennes ont été débutées au moment-même de l'injection des animaux avec des bacilles tuberculeux morts. Ni la 8-azaguanine, ni la l'améthoptérine se sont montrées inhibitoires, quand elles ont été commencées à être injectées souscutanément à la dose de 5 mg/kg et de 2.5 mg/kg respectivement un jour avant l'injection avec des bacilles tuberculeux. Par contre, l'aminoptérine s'est montrée inhibitoire, quand son administration a été débuté pendant la période anté-allergique. Mais, l'allergie tuberculique a commencé à se développer 2 semaines après la cessation de l'administration.
- 2) Chez des lapins, la 6-MP a supprimé le développement de l'allergie tuberculique ainsi que celui des anticorps sanguins tuberculeux, quand elle a été injecté quotidiennement par voie souscutanée à la dose de 10mg/kg.

### Studies on Passive Tuberculin Sensitivity Induced by Cellular Transfer

Ken-ichi YAMAMOTO, Jun ARIMA and Yoshio TAKAHASHI

Spleen cell suspensions originated from donor guinea-pigs sensitized with heat-killed tubercle bacilli (immune cells) and those from normal donor guinea-pigs (normal cells) were transferred to normal recipient guinea-pigs, and the tuberculin hypersensitivity thus induced in these recipient animals was investigated. The following results were obtained.

- 1) The immune cell recipients developed tuberculin skin sensitivity during the first post-transfer period. The sensitivity was found to last for a prolonged period of time when the animals were repeatedly skin-tested with old tuberculin.
- 2) The sensitivity observable during the first post-transfer period is thought to be conferred by transferred living immune cells themselves and to be distinct from the subsequent sensitive state that lasts for many weeks after the first post-transfer week.
- 3) None of the animals that showed intensive, passive tuberculin sensitivity on the 37th day after cellular trans-

fer had antituberculous humoral antibodies such as detectable by means of both the Middlebrook-Dubos test and the passive hemolysis test.

4) The animals given cell suspensions from immune animals which had been desensitized by injection of PPD-s did not develop no or almost no skin reaction during the first post-transfer period. During the late post-transfer period, they developed skin reaction almost same as in control animals which had received non-desensitized cell suspensions.

5) Freeze-thawing and sonic vibration annihilated the capacity of immune cell suspensions to transfer tuberculin sensitivity. Animals given freeze-thawed or vibrated immune cell suspensions produced transitory tuberculin reaction only on the 10th day after cellular transfer.

6) When normal cell recipients were repeatedly tuberculin-tested from soon after cellular transfer, they showed transitory tuberculin sensitivity during first to second week after transfer. On the basis of the facts that (a) protein antigens used other than OT gave rise to no delayed type skin reaction in the recipients, (b) the induced tuberculin reaction was completely suppressed by the intravenous injection of PPD-s, and (c) when tuberculin active peptide (TAP) or tubercle-bacillus polysaccharide (BS-1) were mixed with normal spleen cells and transferred to normal guinea-pigs, passive tuberculin skin reaction appeared only for TAP on the 6th day after transfer but not for BS-1 that has no tuberculin activity, the passive delayed skin reaction obtained in the present experiment is considered to be of typical tuberculin type.

## Immunological Studies on Aspergillosis

### II. Influence of sensitization on experimental aspergillosis

Kaoru KAWACHI

In order to study the role of the hypersensitive reaction on aspergillosis, rabbits previously sensitized with heat-killed aspergilli and normal rabbits were challenged intravenously with living aspergilli, and then at given intervals their lung lesions were observed histologically.

Their serum precipitin titer and skin sensitivity to the protein fraction obtained from culture filtrates of aspergillus were measured and recorded.

1. Until the 5th day after infection little difference could be observed in the intensity of lesions between the sensitized animals and non-treated controls. In the sensitized animals developed in the early stage proliferative inflammatory lesions mainly composed of large mononuclear cells, followed by development of epithelioid granulomata. These lesions were absorbed gradually. On the contrary, in the non-treated controls severe bronchopneumonia constituting of polymorphonuclear infiltration took place from 7 days after infection, changed into proliferative inflammatory lesions.

2. The serum precipitin titer in most of the sensitized animals increased on challenge with living spore, but no correlation was noticed in the intensity of the lesions between the two groups. Direct correlation was shown between the degree of lesions and the intensity of skin sensitivity. However, no clear correlation was obtained between the precipitin titer and the intensity of skin sensitivity.

3. The above results would indicate that the antigen-antibody reaction has a significant role in the development of lung aspergillus lesions.

## Immunological Studies on Aspergillosis

### III. Serum antibodies in aspergillosis

Kaoru KAWACHI

1. Sera from rabbits inoculated subcutaneously with aspergilli were studied electrophoretically. Shortly after infection the beta and gamma globulin fractions increased markedly, and remained increased throughout the experiments.

2. Chromatography on DEAE-cellulose of sera from rabbits sensitized with heat-killed aspergilli detected the existence of various antibody activities.

While the first and second fractions possessed hemagglutinating, precipitating and PCA activities, the third fraction possessed a slight skin-sensitizing capacity.

3. Serum from aspergillosis patient was also fractionated in the same way. Hemagglutinating activity was present in the first and forth fractions, while skinsensitizing activity in the second and third fractions.

## Epidemiological Studies on the Distribution of Atypical Acid-fast Bacillus (Part II)

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This is the second report of the studies on the distribution of atypical acid-fast bacillus (AAB), in Hokkaido which were made with the reaction by tuberculin solutions ( $\pi$ ) purified from AAB (scoto-chromogen strains Ishii and Miike, nonphoto-chromogen strain Gam $\bar{o}$  and photo-chromogen strain P<sub>16</sub>) in contrast to that by human strain H<sub>37</sub>Rv. Tuberculin tests were administered to 477 tbc-inpatients at the two sanatoria in the suburbs of A- and O-city, and 1,253 tuberculin-positive junior high school pupils in S-city.

1. In both the tbc-patient and the pupil groups, the rate of the positive reaction by AAB- $\pi$  was lower than that by <sub>37</sub>Rv- $\pi$  and the positive rate in erythema was higher than that in induration.

2. The proportions of the AAB-positive and H<sub>37</sub>Rv-non-positive were 0.9% to 5.4% in Gam $\bar{o}$ -strain and 0.9% to 1.8% in P<sub>16</sub>-strain in the tbc-patient group, and 0.6% to 1.3% in Miike-strain, 3.2% in Gam $\bar{o}$ -strain and 0.3% to 0.6% in P<sub>16</sub>-strain in the pupil group.

3. In the frequency distribution of the size of erythema, the reaction by AAB- $\pi$  was smaller than that by H<sub>37</sub>Rv- $\pi$  in both groups. The same observations were in the distribution of the size of induration. Especially Ishii-strain showed the weakest reaction in erythema as well as in induration.

4. The number whose reaction by AAB- $\pi$  showed bigger than that by H<sub>37</sub>Rv- $\pi$  was, in tbc-patients, one (0.3%) in Ishii-strain, two (1.9%) in Miike-strain, ten (9.1%) in Gamo-strain and three (2.7%) in P<sub>16</sub>-strain, and, in pupils, eight (2.6%) in Miike-strain, twenty four (7.6%) in Gam $\bar{o}$ -strain and seven (2.2%) in P<sub>16</sub>-strain. The proportion in this category was higher in Gam $\bar{o}$ -strain in both groups compared to that of all Japan.

5. In tbc-patients, the proportion of bigger AAB- $\pi$  reaction than H<sub>37</sub>Rv- $\pi$  was higher in F-type as to the classification of tuberculosis by Gakken and, in Gam $\bar{o}$ -strain, higher in urban district than in rural.

## Pulmonary Diffusing Capacity in the Healthy and the Patient with Various Cardiopulmonary Diseases

Kunio SATO

Diffusing capacity for carbon monoxide ( $DL_{CO}$ ) was measured in patients with various cardiopulmonary diseases by the use of the single breath method. In order to investigate a factors that contribute to the abnormal value for  $DL_{CO}$ , both the membrane component ( $DM$ ) and the pulmonary capillary blood volume ( $VC$ ) were measured separately.

The mean values for  $DL_{CO}$  in normal healthy subjects at rest and during exercise were 22.87 and 28.03 ml/min/mmHg, respectively, showing a positive correlation with the body surface area. The mean normal value for  $DM$  and  $VC$  were 55.8 and 71.4 ml/min/mmHg, respectively.

In patients with pulmonary tuberculosis, the decrease in  $DL_{CO}$  was in parallel with reduction in the ventilatory function and was found to be due to the decrease in  $DM$ . Decrease in  $DL_{CO}$  was also observed in patients with bronchiectasis, in whom both  $DM$  and  $VC$  were found reduced. In bronchial asthma,  $DL_{CO}$ ,  $DM$  and  $VC$  showed only insignificant changes. In case of lung carcinoma, the nearer the location of the tumor towards the hilum, the worse in diffusion capacity. In patients with hilar sarcoidosis,  $DL_{CO}$  was in the normal range. In pulmonary fibrosis, the decrease in  $DL_{CO}$  was in parallel with the decrease in  $DM$ , characteristic to alveolar-capillary block syndrome. Some patients with heart diseases showed a latent reduction in  $DM$ , even though  $DL_{CO}$  was in the normal range.

From the results obtained, it was concluded that separate measurement of  $DM$  and  $VC$  would be necessary for studying pathophysiology of gas exchange in patients with decreased  $DL_{CO}$  value.