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Studies on the Antitubercular Compounds

Shichiro KAKIMOTO, Isao SEKIKAWA, Jun NISHIE,
Ikuko TONE and Ken-ichi YAMAMOTO.
(Research Institute for Tuberculosis, Hokkaido University, Sapporo)

Availability of any antitubercular compounds should be investigated in all the fields of medical sciences, namely bacteriology, physiology, pathology and so on. However, as for the most of the chemotherapeutics prevailing in clinical use, emphasis seems to have been put on their bacteriostatic activities.

The final mechanism of action of the tuberculostatic compound is thought to be a chemical reaction between the compound concerned and the tubercle bacillus. Therefore, first of all, the relation between the chemical constitution and its activity against tubercle bacilli must be clarified in vitro.

The author has supposed that there may exist two different chemical groups in the molecule of any one of antitubercular compounds; one is a group having affinity for the tubercle bacillus, and the other a group having noxious action against it.

In order to prove this supposition, several kinds of compounds have been prepared, in which the existence of cross-resistance has been tested for one another. Thus, it has been clarified that tubercle bacilli exhibit resistance to the acting group of a compound and not to the affinitive group. On the basis of this fact, several new active compounds have been theoretically synthesised.

Allergic Reaction in the Lungs-An Immunopathological Study

5. Reaction Against the Fraction of Myc. tuberculosis

K. KAWACHI and M. TOMISAKI

Rabbits previously sensitized with heat-killed tubercle bacilli, tne proteolipid fraction (Folch), or the tuberculin protein fraction was injected intratracheally with the saline emulsion of the proteolipid fraction (100 γ). Their lungs were studied histologically at given intervals.

The control normal rabbits injected with the proteolipid fraction showed a severe but transient pneumonia mainly composed of large mononuclears, followed by complete absorption a week after injection. On the other hand, in the rabbits sensitized with killed bacilli a great number of premature tubercles were formed from the first day of the proteolipid injection. Epithelioid-cell tubercles were completed on the 10 th day. Simillar aspect in the development of the lesion was also observed in the rabbits sensitized with the proteolipid fraction. The lesions of this group were severer than those in the rabbits previously sensitized with killed bacilli and later challenged with killed bacilli (2 mg). However, in the rabbits sensitized with tuberculin protein the proteolipid fraction provoked less severe productive inflammation.

As control experiments, rabbits sensitized with heat-killed tubercle bacilli and normal rabbits were injected intratracheally with the phosphatide fraction (antigen for Takahashi's kaolin-agglutination reaction). Only weak productive changes were observed in both sensitized and nonsensitized animals.

These data would indicate that the proteolipid of the tubercle bacillus plays a very important role in the formation of epithelioid-cell tubercles.

Allergic Reaction in the Lungs-An Immunopathological Study

6. Discussion and Conclusion for the Series of Preceeding Reports

K. KAWACHI and K. MORIKAWA

In the series of preceeding papers histopathological studies of the pulmonary lesion evoked in normal or specifically sensitized rabbits by intratracheal injection with either specific protein antigens, or non-specific foreign bodies, or fractions of tubercle bacilli were reported.

From these data attempts were made to find the histogenesis of productive lesions in tuberculosis, especially the development of epithelioid cells.

The development of tuberculoid lesions composed of epithelioid cells seems to need a definite condition. If the condition was satisfied, these lesions can develop, though slightly, even following a simple inflammatory stimulation, which is known by the name of "foreign body stimulation". However, this simple stimulation of foreign bodies alone was found to be insufficient as a causal factor of the epithelioid lesions in tuberculosis. Even the phosphatide or proteolipid fraction of tubercle bacilli did not evoke such lesions in normal rabbits, while it did in sensitized rabbits.

Thus, the antigen-antibody reaction can be said to play the most important role in the development of tuberculoid lesions.

These interpretation would throw some light on the pathology of diseases characterized with the formation of tuberculoid lesions, such as sarcoidosis, brucellosis and turalemia etc.

Study on Temporary Desensitization in Tuberculosis following Intravenous Injection with Tuberculoproteins.

Susumu NISHIYA

In order to clarify the mechanism of development of tuberculous allergy, experiments on desensitization following intravenous injection with tuberculoproteins were conducted in guineapigs and rabbits experimentaly infected with dead or living tubercle bacilli.

In the guineapigs infected with living tubercle bacilli, repeated subcutaneous injections of tuberculoproteins started on the day of infection did not suppress the development of cutaneous tuberculin allergy.

In the guineapigs and rabbits strongly sensitized with dead tubercle bacilli, one single intravenous injection of tuberculoproteins completely suppressed for 3 to 4 days the development of the tuberculin skin reaction, when the injection was performed one hour before the skin testing. The same was true when tuberculopolypeptides were used for intravenous injection. On the contrary, intravenous injections of tuberculopolysaccharides showed no suppressing effect on the skin reaction.

As for PPD-s, the minimum dose effective for suppressing temporarily the tuberculin skin reaction was from 50 to 100 μg.

In the rabbits sensitized with dead tubercle bacilli, no correlation was found to exist between temporary desensitization on the one hand and circulating antibodies (antiprotein, antipolysaccharide and antiphosphatide), complement and the serum protein fractions on the other.

Repeated intravenous injections of tuberculoproteins were found to have almost no influence on the

development of tuberculosis in guineapig infected with living tubercle bacilli.

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

E. TAKAKUWA, M. ONO, S. KAWAMURA,
(Department of Hygiene and Preventive Medicine, Hokkaido University School of Medicine
S. ARISUE
(Hokkaido Medical Affairs Bureau, Welfare Ministry)
K. KONDO
(National Daini Sanatorium)
M. OKUDA
(Nakanoshima Chūō Hospital)
T. ITŌ
(Hokkaido Kōsai Sanatorium)
Y. MIYAGI
(National Sapporo Sanatorium)

The distribution of the atypical acid-fast bacillus (AAB) in Hokkaido was observed with the reaction by tuberculin solutions (π) purified from AAB (scoto-chromogen strain Ishii, nonphoto-chromogen strain Gamō, photochromogen strain Bostrum and avian strain A_{71}) in contrast to that by human strain $H_{37}Rv$. For the purpose of this study, tuberculin tests were administered to 357 tbc-inpatients at the four sanatoria in the suburbs of S-city and 546 tuberculin-positive junior high school pupils at E-village.

1. In both the tbc-patient and the pupil groups, the rate of the positive reaction by AAB-π was very low in comparison with that by $H_{37}Rv$.

2. The proportions of the AAB-positive and $H_{37}Rv$-non-positive were 1.3% in Bostrum-strain and 1.1% to 2.2% in A_{71}-strain in the tbc-patient group, and 0.8% in Gamō-strain as well as in A_{71}-strain in the pupil group.

3. In the frequency distribution curves of the size of erythema, both the tbc-patient and the pupil groups showed the distribution with the peak in 2 to 5 mm in the reaction with AAB-π, which was smaller diameter in erythema than that with $H_{37}Rv$.

4. The proportion of the recognizable induration with AAB-π was very low in both groups compared to that with $H_{37}Rv$.

5. In tbc-patients, the number whose reaction with AAB-π showed bigger than that $H_{37}Rv$ was, in erythema, one (1.1%) in Gamō-strain, two (2.6%) in Bostrum-strain and one (1.1%) in A_{71}-strain, and, in induration, one (1.1%) in Gomō-strain, one (1.3%) in Bostrum-strain and two (2.2%) in A_{71}-strain. This figure means no special difference in comparison with that of all Japan.

In pupils, the number whose reaction with AAB-π showed bigger than that with $H_{37}Rv$ was, in erythema, one (0.7%) in Ishii-strain, one (0.8%) in Gamō-strain and one (0.8%) in A_{71}-strain, and, in induration, was nothing in each strain. This figure means also the same as that all over Japan.

These results suggested that AAB infection could not be denied in Hokkaido, but the number of cases are very few.