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Considerations on the Experimental Data so far Obtained by Numerous Workers in the Study of Tuberculous Allergy

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The existing theories on the relation between allergy and immunity in tuberculosis can be divided into two different views quite opposite to each other; one regards both allergy and immunity as being based on the same mechanism, the other regards them as two different phenomena, each being based on an unrelated mechanism.

The former view stands on the experimental data that allergy and immunity run consistently in parallel with each other, while the latter view stands on the fact that they are observed to be dissociable. The author discussed, in this paper, how to interpret the experimental data so far reported by numerous workers and has attempted to point out the paralogism existing in the two views mentioned above.

Studies on the Virulence of Atypical Mycobacteria

Jun ARIMA, Ken-ichi YAMAMOTO and Kazuo MORIKAWA

Comparative study was made on the virulence of atypical mycobacteria. Use was made of 18 strains, comprising 5 photochromogenic, 6 scotochromogenic, 6 non-photochromogenic strains and 1 rapid-grower. Evaluation of the virulence was performed by three tests: the tissue culture test, the guinea-pig inoculation test, and the mouse inoculation test. The results obtained were as follows:

1) In the tissue culture test, the majority of the strains revealed markedly low virulence. Of these strains, however, several ones showed themselves moderately virulent. This might be due to the invasive ability of the bacilli for the tissue cells in the early stage of infection.

2) While all the strains tested were avirulent for the guinea-pig, they showed a certain degree of pathogenicity for the mouse.

Studies on the Effect of Adjuvant on Tuberculous Immunity.

1. Difference in the Effect of Adjuvant on Living and Nonviable Vaccines

Nobuyuki TERAMOTO and Yukio YAMADA

In this experiment, living BCG vaccine was demonstrated to give considerably less protection in mice against tuberculous infection when it was administered in adjuvant than when it was suspended in saline. This finding is in contrast to that obtained with killed vaccine prepared from tubercle bacilli, the immunizing potency of which has been reported to be enhanced by adjuvants. No explanation for this paradoxical finding could be given, since the adjuvant used was found to stimulate the growth of BCG

in mice instead of showing any inhibitory effect which would reduce the immunizing potency of BCG vaccine.

On the Qualitative and Quantitative Determination of Supplementary Fluids for Lung Resection

— a Mixture of 5 per cent Glucose and Physiological Saline Solution (2 : 1) —

Tomio GOCHO

With the intent of clarifying the significance and value of a mixture of 5 per cent glucose and physiological saline solution as a supplementary fluid in lung resection, the author selected 11 male tuberculous patients.

Studies were centered on the measurement of urine quotient (O/K_4) and measurements were made on various biological substances in urine and blood.

Conditions of transfusion for the above solution: 1500 cc during and on the day of operation, 1000 cc on the 1st post-operative day, 500 cc on the following day, a total of 3000 cc.

Conditions of blood infusion: Bank blood was infused during and after operation in approximately the same volume as blood lost.

Results: Pre- and post-operative fluctuations in the urine quotient were as follows:

2 day prior to op.	34.9± 1.95	4 th day after op.	47.6± 4.10
1 day prior to op.	34.9± 1.60	5 th day after op.	40.1± 2.54
Immediately after op. (0 day)	169.0±44.93	7 th day after op.	55.1± 6.09
1 st day after op.	54.5± 5.65	9 th day after op.	39.9± 2.84
2 nd day after op.	60.6± 7.89	12 th day after op.	56.9±11.13
3 rd day after op.	53.0± 7.86		

I) The 11 subjects were divided into high and low quotient value groups based on the values at 0 day. The mean values of both groups were 352.3±92.23 and 70.8±21.60.

It was noted that the high group showed high values in loss of blood (2000~1000 cc) during and 0 day after operation and significantly high values in urine potassium at 0–4 th days after operation.

II) The subjects were redivided into high and low at 2–4 days after operation. The mean values of both groups were 71.4±7.12 and 40.2±1.40.

The high group showed high values in loss of blood (2200~1200 cc) during and 0 day after operation, low values in serum potassium and high values in serum sodium at 2–4 days after operation.

III) The subjects were redivided into high and low at 9–12 days after operation. The mean values of both groups were 60.7±10.56 and 36.8±1.72.

The high group showed high values in blood loss (2800~1700 cc) at 0–4 days after operation, low values in serum potassium, high values in serum sodium, low values in haematocrit and high values in urine O/N at 9–12 days after operation.

IV) A comparison between lung resection (the author) and thoracoplasty (Oda) at 0 day after operation under the same transfusion conditions: In the author's group, high values in O/K_4 and urine sodium, low values in urine chlorine, blood potassium and blood chlorine were seen.

Now if it can be assumed that the above urine quotient method is a '*Human Vitality Criterion*', the above results may be summarized as follows: In lung resection the present 2 : 1 mixed transfusion brings about a remarkable loss in potassium in subjects in whom a large amount of blood is lost. This is due to the sodium excessively contained in the transfusion.

Thus it is suggested that, while the present transfusion may be excellent for thoracoplasty, there is much room left for improvement in regards to lung resection.

Experimental Study on the Antigenical Diversity of Tuberculoprotein

Harue OKUYAMA, Akihiko OHTA and Kazuo MORIKAWA

In order to clarify the antigenicity of tuberculoprotein, zone electrophoresis and DEAE-cellulose fractionation were conducted for a tuberculoprotein precipitated from non-heated filtrates by trichlor acetic acid at pH 4.0.

The zone electrophoretic patterns showed one protein, three hoxose and two pentose peaks. The mobility of both carbohydrates was lower than that of the protein.

Substances active in eliciting tuberculin skin reaction existed around the protein peak. Skin activity of the fractions was parallel to their protein concentration. Boyden hemagglutination tests ran also parallel in intensity to the protein concentration. On the other hand, precipitin tests, Middlebrook-Dubos hemagglutination and hemolysis tests had a close relation to the polysaccharide concentration.

However, as for the fractions obtained by the DEAE-cellulose fractionation, precipitin and skin tests had a close relation to their protein concentration: protein fractions containing no polysaccharide which evoked strong skin reactions in tuberculous rabbits were shown at the same time to give good precipitin reactions in the contact of tuberculous serum.

A protein fraction which was mixed with antisera in equivalent volume to give no longer precipitation reaction did evoke a strong skin reaction in tuberculous rabbits.

This fact would indicate that tuberculoprotein contains two different antigenic components: antigen for precipitation and antigen for skin reaction.

Periodical observation of the sequences of the skin reaction disclosed that an antigenic component which elicite the tuberculin reaction of the immediate type was contained in a DEAE-fraction.

Centrifugal analyses showed that tuberculoproteins of almost all fraction had an identical sedimentation constant, but a fraction which contained protein in the highest concentration had a high sedimentation constant.

From these results the antigenicity of tuberculoprotein was discussed.

Allergic Reaction by Tuberculin Protein and Polysaccharide

Kazuo MORIKAWA, Harue OKUYAMA and Masako TOMISAKI

Rabbits were injected subcutaneously with several tuberculin protein and polysaccharide fractions for verifying their antigenicity. Thirty days after injection they were skin-tested and the sera were obtained for measuring precipitin titers. Afterwards they were injected intrapulmonarily with these fractions mixed with adjuvant. Necropsy was made 30 days after the intrapulmonary injection.

These two kinds of fractions produced specific antibodies to themselves, as well as those, though slightly, to the alternate antigens.

Intrapulmonary injection caused to develop a severe allergic reaction in the lungs. However, the polysaccharide fraction was more active in developing cavitary lesions than the protein fraction. Histologically, the protein fraction produced a productive change accompanied mainly with monocytes and epithelioid cells. The polysaccharide fraction caused an exudative change accompanied with an intense polymorphonuclear infiltration.

Study on the Cavity Formation in Experimental Animals—Intrapulmonary Injection with Tuberculin Polysaccharide, Ovalbumin or Myc. phlei

Kazuo MORIKAWA, Harue OKUYAMA, Kaoru TSUGE and Akihiko OHTA

In order to verify the causative factors in the development of cavitary lesion in animals, tuberculin polysaccharide, ovalbumin or heat-killed Myc. phlei were injected into the lungs of sensitized or non-sentisitized rabbits. Up to 30 days after injection the animals were killed at regular intervals and the pulmonary lesions were observed.

The following results were obtained:

1. Cavitary lesions developed only in sensitized animals.
2. Under the present condition tuberculin polysaccharide caused cavitary lesions more frequently did living tubercle bacilli.
3. Almost no direct correlation was found between the development of cavity and the grade of hypersensitivity as estimated from skin reactions and serum antibody titers.
4. Lesions engendered by injection with tuberculin polysaccharide were especially localized and composed with only necrosis and cavity, without peripheral tuberculous lesion.
5. In the sensitized rabbits intrapulmonary injection of ovalbumin caused necrotic lesions accompanied by severe polymorphonuclear infiltration, which were different from tuberculous hypersensitive reaction.
6. In the sensitized animals heat-killed Myc. phlei developed cavitary lesions with abundant epithelioid tubercles. These findings were almost indistinguishable from those engendered by heat-killed tubercle bacilli.