

Dextran Reactive Antibody : Its Titre Distribution in Japanese

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ABSTRACT. Two hundred forty-one samples of serum collected randomly from patients undergone surgical procedure in Central Operation Unit, Kawasaki Medical School Hospital from October 1980 till January 1981. Titre of dextran reactive antibody (DRA) in the serum was determined by passive hemagglutination method. No DRA was detected in 114 (56.4 %) out of the 241 serum and DRA was found in the remained 127. Titres of DRA distributed in a normal distribution form with mean of 2^{5.27} in the latter group. The titres seemed to decrease slightly corresponded to aging. No difference was found in distribution of titres between both sexes. Distribution of titres in serum which was obtained from subjects who were experienced infusion of dextran solution or who were supposed to be was most likely comparable with that in the whole subjects. No correlationship between DRA titre and allergic diathesis was noted in this study.

Several papers have been reported about allergic or anaphylactic reaction occurred following infusion of dextran solution since the first experience was informed by Getzen¹⁾.

Ring & Messmer²⁾ collected 85,882 cases who were infused dextran solution in 31 hospitals in Southern Bavarian in 1975. Twenty-eight cases (0.032%) out of them developed to anaphylactic or anaphylactoid reaction. Recently Grabar³⁾, Kabat & Berg⁴⁾ demonstrated that dextran reactive antibodies (DRA) exist naturally in a certain percentage in human serum. Hedin⁵⁾ collected 123 samples of serum from patients, who developed to dextran induced anaphylactid reaction (DIAR), and determined distribution of DRA titre. They demonstrated that high titre of DRA corresponded not intimately to incidence or severity of DIAR.

On the other hand, in Japan, none of DIAR has been reported in the last decade except Sasaki's paper⁶⁾ appeared in 1970. One of the authors (M. T.) has never experienced DIAR for the recent 14 years while he used to infuse dextran solution for blood volume replacement in 1/5-1/6 of all cases with surgical procedure. Therefore we felt that a certain difference might exist in dextran immunization or in distribution of titre of DRA between Caucasian people and Japanese. In this study we collected serum randomly from 241 patients

who were performed surgical procedure and analyzed its DRA titre by technical assistance of Dr. Richter, W., in Pharmacia, A.B., Uppsala, Sweden. And then we compared distribution of DRA titre in Japanese people with that in European.

MATERIALS AND METHODS

Blood of eight milliliters was collected randomly from 241 patients who were done surgical procedures under general anesthesia in Central Operation Unit, Kawasaki Medical School Hospital from October, 1980 till January, 1981. The blood was transferred in a 15 ml glass test tube and kept in a refrigerator at 5°C for 6-8 hours for separation of serum. The serum was frozen and sent to Biochemical Research Laboratory, Pharmacia A.B. DRA titre in the serum was determined by passive hemagglutination method⁵⁾.

After the blood sampling, 10 ml of dextran 70 solution or 500 ml, if necessary, was infused into the patients and changes in their circulatory dynamics, respiratory resistance and skin reactions were observed clinically.

The patient's past history, particularly referred to previous operation or trauma and to asthma, atopic dermatitis or allergic reaction, was recorded precisely and compared with their own DRA titre.

RESULTS

No DRA was found in 114 (56.4%) samples out of 241 and DRA titre, frequency of which appeared in a normal distribution form from 2^1 to 2^{14} , was found in the remained 127 samples, as shown in Figure 1. No difference between the both sexes was noted in the distribution of DRA, namely value of $2^{5.15} \pm 2^{1.84}$ in the male and of $2^{5.43} \pm 2^{2.38}$ in the female. The relationship between age of the subject and DRA titre is shown in the Figure 2. No significant correlation was found between those parameters while titre of DRA seemed to decrease slightly paralleling to aging. Both high titre of 2^{14} and 2^{12} were found in two patients who were operated partial gastrectomy for peptic ulcer of the stomach. Positive or suspectable history of previous administration of dextran solution was recorded in 35 patient in this study. In 22 of them, however, no DRA was found and DRA was found in the remained 13. The DRA titres distributed from 2^1 to 2^9 and their mean values and standard deviation was $2^{6.03}$ and $\pm 2^{2.43}$, respectively. These distribution was most likely comparable with that of $2^{5.18} \pm 2^{2.04}$ in the remained subjects.

Twenty-two patients who had history of asthma, urticaria or allergic reactions were found in the whole 241 subjects. No DRA was detected in 12 patients out of 22 and DRA was found in the remained 10 patients. Distribution of the DRA titre was also mostly comparable with that of the whole group. Namely mean of the DRA titre of those 12 patients was $2^{4.30}$ and its standard deviation was $\pm 2^{2.67}$. None of adverse reactions, such as bronchospasm, hypotension, skin rash etc., was observed throughout the study.

Number of individuals on the ordinate

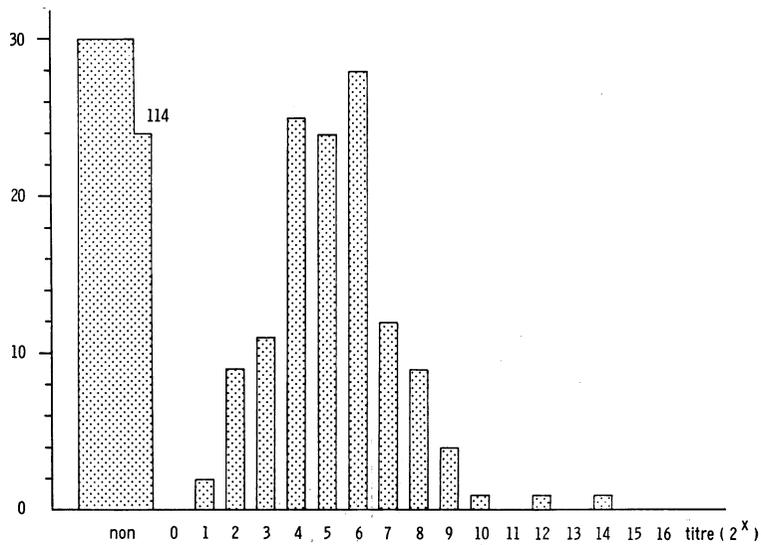


Figure 1. Distribution of DRA titres (n=241)

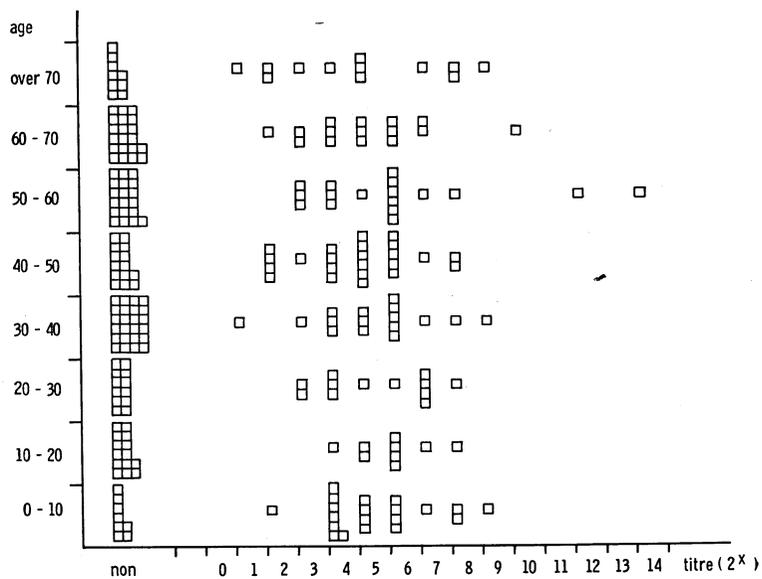


Figure 2. Relationship between titres and ages.

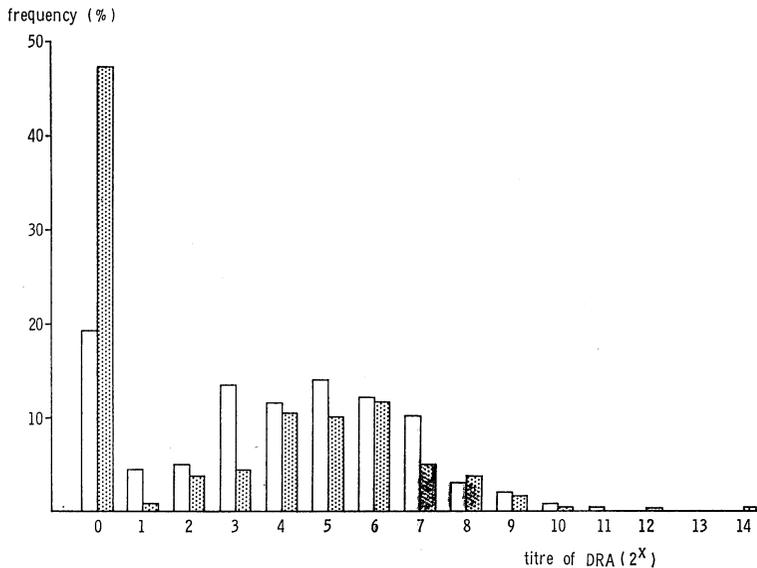


Figure 3. Comparison between distribution of DRA titres in Japanese (■) (n=241) and in Caucasian (□) (n=1408). Distribution of DRA titre in Caucasian was studied by Dr. Richter, W.⁷⁾

DISCUSSION

The distribution of DRA titre in Japanese people appeared mostly comparable with that observed in Caucasian people by Richter⁷⁾, as shown in the Figure 3. However the frequency of null titre in the Japanese was significantly higher than that in Caucasian ($p < 0.001$). It may explain why DIAR will be experienced in clinical practice relatively uncommonly in our country. Distribution of DRA titres seemed to tend to decrease slightly paralleled to ages. It might attribute to general diminution of antibody production in aged. Richter⁵⁾ concluded that DIAR were not only mediated by dextran-specific reagins but also by combination of many factors. It has been documented, nevertheless, that high titres were observed more frequently in patients with severe DIAR. Jacobsson⁸⁾ experienced 2 mild DIAR in 44 volunteers with high titres. Richter speculated that circulating DRA-dextran complexes might trigger cascade reactions via plasma anzyme system and thereby would elicit DIAR in predisposed individuals⁵⁾.

In this study, no correlationship was observed either between the distribution of DRA and the ages or between the former and the sex. No DIAR was experienced in this study while the dextran challenge was done in every subject. The dextran challenge in this study was done under general anesthesia which was believed likely to lessen an incidence of anaphylactoid reaction or to reduce

its severity. Richter⁵⁾ observed, however, a high incidence of severe reaction following intraoperative infusion of dextran solution. He realized also that anesthetic technique or agents did not effect on the incidence of DIAR. A review on all aspects of dextran hypersensitivity including its mechanism and specific prevention has recently been published by Richter and Hedin⁷⁾. Many mechanisms are assumed for natural DRA production. One of the most possible source for immunization has been supposed to attribute to dextran or other polysaccharides fermented in the gastrointestinal lumen by microorganisms. And these polysaccharides could permeate easily through the luminal wall and enter into the blood stream when local inflammation or injury existed. Relatively high titres were found in the patients in this study both who had suffered from peptic ulcer of the stomach with pyloric stenosis. This high titre immunization might be caused by the mechanism mentioned above.

It has been reported that a single infusion of dextran solution increases titre of DRA within 1-140 weeks⁵⁾. In this study, however, no difference was noted in distribution of DRA titres between the subjects with dextran infusion and subjects without infusion. We have felt that natural immunization contributes to incidence of DIAR more dominantly in clinical practice and single infusion of dextran solution does in less extend.

Acknowledgment

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The data obtained in this study has been reported to W. H. O. by Dr. Richter, W.

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