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**ANTIGAMMA-GLOBULIN FACTORS AND LEVELS OF IgG,
 IgA and IgM IN SERA OF PATIENTS WITH DUPUYTREN'S
 CONTRACTURE**

K. NOEVA, S. KARAGANTCHEVA, A. S. TOSHKOV

Antigamma-globulin factors were detected as a feature of many infectious and non-infectious diseases, although the reason of their formation has not yet been determined. The presence of these antibodies is mostly connected with progression of autoimmune processes. A part of organisms' own IgG is structurally changed, acquires an antigenic character and triggers formation of antibodies. This hypothesis is corroborated by existence of experimentally induced antigamma-globulin factors. Other authors consider these factors as antibodies directed against complexes antigen-antibody, which are circulating in blood stream during infectious processes.

A discovery of antigamma-globulin antibodies by chronic diseases with unclear etiology and pathogenesis deserves a special interest. One of such diseases is Dupuytren's contracture affecting the palmar connective tissue of the hand. No hypothesis explaining the pathogenesis of the contracture of fingers, suggested during more than one hundred years, was generally accepted. Some more recent data are in favour of suggestion that autoimmune processes may play a role in the development of the disease. Therefore, it was of interest to examine, if such antibodies are present in sera of patients with Dupuytren's contracture, having in mind possible autoimmune character of the antigamma-globulin factors.

In this study, the content of antigamma-globulin factors and immunoglobulins IgG, IgA and IgM were estimated in blood sera of patients with Dupuytren's contracture, thus enabling description of a state of humoral immunity in this disease.

MATERIALS AND METHODS

1. Sera were obtained from 102 men suffering from Dupuytren's contracture and treated in the Institute of Orthopaedics and Traumatology. Depending on severity of the contracture, positive family history and accom-

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Tab. 1

Distribution of the examined sera in respect to groups and age of the patients with Dupuytren's contracture

Group	Age				Total
	less than 40 years	from 41 to 50 years	from 51 to 60 years	more than 60 years	
I	1	2	10	8	21
II	1	5	11	11	28
III	5	11	16	21	53
Control	7	18	37	40	102

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panying alterations of the connective tissue, the patients were divided into three groups:

The first group: The patients with initial nodose stage of Dupuytren's contracture, negative family history, without signs of Lederhose's disease and lacking subcutaneous nodules in joints of fingers of the hand.

The second group: The patients with flexion contracture of fingers, negative family history and without nodules in joint of fingers.

The third group: The patients with flexion contracture of fingers, positive family history and accompanying alterations of the connective tissue (Lederhose's disease and nodes).

The numbers of the examined sera are shown in Tab. 1, in dependence on age of patients. Sera obtained from 102 normal donors of the corresponding age were examined simultaneously.

2. Pure IgG fractions were prepared from commercial human and pig gamma-globulins — Cohn's II fraction by means of chromatography on DEAE-cellulose.

3. Using bis-diazo-benzidine for binding of IgG, the soluble aggregates of human and pig IgG were obtained. Diazo-benzidine-IgG was purified by chromatography on DEAE-cellulose.

4. Agar immunodiffusion was performed in 1 per cent agarose in 0.06 M Veronal buffer, pH 8.6.

5. Heterohaemagglutination reaction according to Waaler Rose. If a haemagglutination occurred in dilutions of serum higher than 1:56, the titre was considered as positive.

6. The content of IgG, IgA and IgM immunoglobulins in the examined sera was estimated by the radial immunodiffusion method of Mancini et al. (1965). The monospecific anti-human IgG, IgA and IgM antisera, which were prepared in the Centre of Infectious and Parasitic Diseases (Sofia), and standard immunoglobulin serum for IgG, IgA and IgM testing produced by "Sevak" (Czechoslovakia), were used. Very precisely calibrated pipettes, available for quantitat-

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Tab. 2
Antigamma-globulin factors in sera of patients with Dupuytren's contracture

Group	Precipitation with aggregated IgG				positive per cent
	human		pig		
	+	-	+	-	
I	-	-	6	15	28.5
II	-	-	14	14	50.0
III	-	-	39	14	73.5
Control	-	-	32	70	31.3

ive immunodiffusion and produced by "Hyland" (Swis), were used for pipetting of sera. In each hole of an agar plate 0.04 ml of serum was applied.

RESULTS AND DISCUSSION

I. Antigamma-globulin factors

The sera of patients with Dupuytren's contracture were examined. The results of the immunoprecipitation indicated the presence of heterospecific antigamma-globulin factors in sera of patients of the IInd and the IIIrd group in significantly higher percentage than in control subjects. These factors precipitated an aggregated pig IgG, but did not lead to precipitation of aggregated human IgG (Tab. 2).

By patients with nodose stage of the disease and negative family history (Ist group of patients) the percentage of the formation of antigamma-globulin antibodies was not higher than in the controls (28.5 per cent and 31.3 per cent, respectively).

By patients of the IInd group with expressed flexion contracture, the antigamma-globulin factors were revealed in 50 per cent of the examined sera.

Tab. 3
Waler Rose titres in sera of patients with Dupuytren's contracture

Group	Waler Rose titres							positive per cent
	negative				positive			
	7	14	28	56	112	224	448	
I	3	6	6	4	2	-	-	9.5
II	4	12	8	3	1	-	-	3.3
III	5	14	23	6	5	-	-	9.0
Control	29	37	23	9	4	-	-	3.9

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By patients of the IIIrd group with flexion contracture, positive family history and alterations of the connective tissue, the antibodies were found in 73.5 per cent of the cases.

All these facts are indicating, that formation of antigamma-globulin factors is connected with progression of the disease and with systemic character of the pathologic changes in the connective tissue.

The negative titres of Waaler Rose reaction were obtained in more than 90 per cent of the sera examined in all three groups of the patients (Tab. 3), i. e. the antigamma-globulin factors present in sera of the patients with Dupuytren's contracture do not possess heterohaemagglutinating properties.

It is known that reactions of heterohaemagglutination are proving a presence of antigammaglobulin antibodies belonging to the IgM group. The ab-

Tab. 4
The levels of IgG, IgA and IgM in sera of patients with Dupuytren's contracture

Immuno- globulins	I st group		II nd group		III rd group	
	Patients	Controls	Patients	Controls	Patients	Controls
IgG						
Mean value	1910 ± 77	1510 ± 53	1780 ± 60	1430 ± 57	1850 ± 56	1550 ± 48
Interval	1290—2540	820—183	1090—2530	960—2030	990—2670	1050—2200
p	0.001		0.001		0.001	
IgA						
Mean value	449 ± 21	387 ± 22	451 ± 34	367 ± 18	423 ± 16	346 ± 15
Interval	320—672	224—640	167—790	234—589	198—689	160—604
p	0.05		0.025		0.001	
IgM						
Mean value	103 ± 7	90 ± 7	77 ± 6	89 ± 6	91 ± 6	94 ± 5
Interval	47—163	46—144	44—152	46—160	41—227	44—204
p	0.20		0.20		0.70	

sence of Waaler Rose titres in our case leads to suggestion, that antigamma-globulin factors of patients with Dupuytren's contracture belong to the IgG type. It may be supported by the stable content of IgM and increased levels of IgG in majority of the examined sera (Fig. 1).

We found no data in literature on levels of antigamma-globulin factors by patients with Dupuytren's contracture. It was revealed in our study that they are formed especially by a severe form of the disease, connected with genetic load and systemic affection of the connective tissue. The antibodies are heterospecific as they precipitate with aggregated pig IgG. It would be of interest to follow dynamics of their level and to prove their immunoglobulin nature.

II. Immunoglobulins

and IgM — in sera of 102 patients, some information in respect to the state of the humoral immunity by Dupuytren's contracture was obtained. The results are shown in Fig. 1. Above the normal level of IgG was found in 46.7 per cent of the sera of group I patients, in 39.3 per cent of group II patients and in 47.1

per cent of group III patients. Approximately, in one third of all examined patients an IgA content in serum was higher, compared to the controls. In three patients of the IInd group the values were higher than 750 mg/100 ml.

No changes of IgM content were observed. In all examined cases, with exception of insignificantly increased values in three patients of the IIIrd group, the content of IgM remained within normal limits.

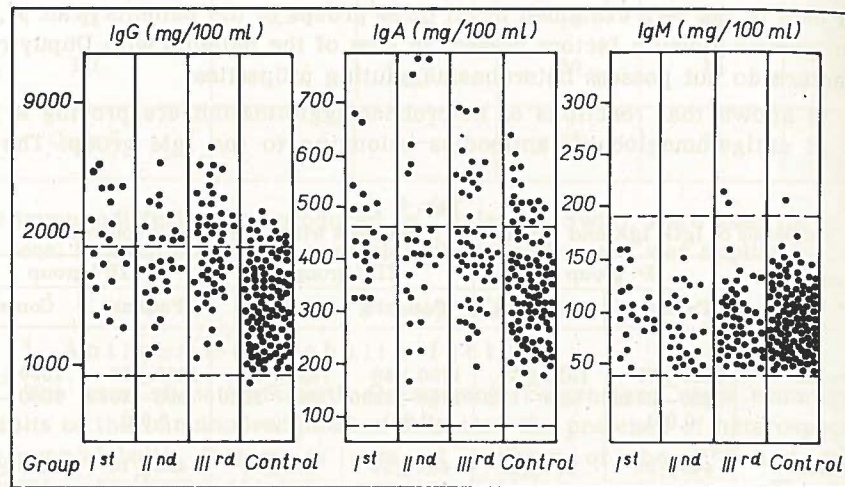


Fig. 1 — Serum immunoglobulins in patients with Dupuytren's contracture of the Ist, IInd and IIIrd group, and in normal donors (control).

Average contents of IgG, IgA and IgM, the standard deviation (SD) and the statistic limits of significance (p) in the sera of the examined patients and in corresponding control sera of the normal donors, are shown in Tab. 4.

The mean concentration of IgG by patients of all three groups was significantly higher than by controls. The difference of increased values is statistically significant (p = 0.001). Statistically significant are also the increased levels of IgA in all three groups of the examined patients (P=0.05, 0.025, 0.001, respectively).

A possible dependence of the increased levels of immunoglobulins IgG and IgA on other diseases could be excluded in this study, as majority of patients with Dupuytren's contracture were otherwise healthy. Only some patients had ulcus disease and hypertony, i. e. diseases lacking a direct relationship to the state of humoral immunity.

The changes of the serum immunoglobulins in patients with Dupuytren's contracture are also referred by Gay and Gay. In 12 patients examined increased levels of IgG were found.

Our results show a distinct and statistically significant increase of IgG and IgA levels in sera of patients with Dupuytren's contracture. Greater

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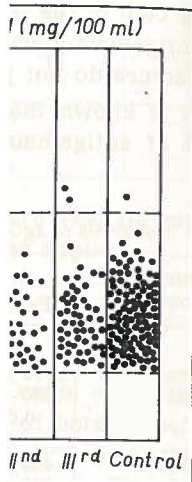
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differences in the state of the humoral immunity by slight (Ist group of patients) and severe (with relapses) forms of the disease, were not observed. The mean values of IgG and IgA levels in all three groups of patients were very close. Therefore, the increased IgG and IgA levels may serve as a supplementary parameter by the determination of the disease. However, no information can be drawn from their changes in respect to the severity of the disease.

CONCLUSIONS

1. Heterospecific antigamma-globulin factors in sera of patients with Dupuytren's contracture are found especially in cases with severe form of the disease, i. e. if flexion contractures of the fingers, genetic load and systematic alterations of the connective tissue are present.

2. Increased levels of serum immunoglobulins IgG and IgA were observed, while IgM content remained within normal limits. M. T.

SUMMARY

The content of antigamma-globulin factors in the sera of 102 patients with Dupuytren's contracture was estimated. The presence of antibodies reacting heterospecifically with aggregated pig IgG was proved especially in cases with severe form of the disease (73.5 %). The level of the serum immunoglobulins IgG, IgA and IgM was determined by all examined patients. The increased levels of IgG and IgA were found.

RÉSUMÉ

Facteurs d'antigamma-globuline et le niveau IgG, IgA et IgM dans le serum des malades atteints d'une contracture de Dupuytren

M. Noeva, S. Karagantcheva, A. S. Tochkov

On a observé les facteurs d'antigamma-globuline dans le serum de 102 patients atteints d'une contracture de Dupuytren et même prouvé la présence des anticorps réagissant de manière hétérospécifique avec les IgG agrégés du porc, surtout dans les cas graves de cette maladie (73,5 %). Chez tous les examinés on a établi le niveau des immunoglobulines de serum IgG, IgA et IgM. Nous avons constaté le contenu élevé de IgG et IgA.

ZUSAMMENFASSUNG

Antigammaglobulinfaktoren und der Spiegel von IgG, IgA und IgM im Serum von Patienten mit Dupuytren'scher Kontraktur

K. Noewa, S. Karagantschewa, A. S. Toschkow

Es wurde untersucht der Gehalt an Antigammaglobulinfaktoren im Serum von 102 Patienten mit Dupuytren'scher Kontraktur. Wir bewiesen das Vorhandensein von Antikörpern, die mit aggregierten IgG des Schweines heterospezifisch reagieren vor allem in Fällen der schweren Erkrankungsform (73,5 %). Bei allen untersuchten Patienten bestimmten wir den Spiegel von IgG, IgA und IgM. Es wurde ein erhöhter Gehalt an IgG und IgA gefunden.

RESUMEN

Factores de antigamaglobulina y el nivel IgG, IgA y IgM en el suero en los pacientes con la contractura de Dupuytren

K. Noeva, S. Karagancheva, A. S. Toshkov

Fue observado el contenido de los factores de antigamaglobulina en el suero de 102 pacientes afectados de la contractura de Dupuytren. Fue probada la presencia de anticuerpos que reaccionan de manera heterospecifica con las IgG agregadas del puerco, sobre todo en los casos de la forma grave de la enfermedad (73,5 %). El nivel de las inmunoglobulinas IgG, IgA y IgM fue determinado en todos los examinados. Un contenido elevado de IgG y IgA fue probado.

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To commemorate 25 years of the activity of the oldest European Tissue Bank in Hradec Králové — ČSSR the scientific meeting will take place in Hradec Králové from 12th to 15th September 1977, organized by Czechoslovak Academy of Science and Regional Institute of Public Health in Hradec Králové.

Programme:

1. Terminology of cryobiology (open discussion of the C-1 Commission of the Inst. Inter. of Refrigeration)
2. Sterilization of tissue grafts by means of ionizing radiation (the collaboration with Int. Atomic Energy Agency is expected)
3. Long-term preservation of tissue grafts (laboratory and/or clinical results)
4. Freeze-drying
5. Miscellaneous

Languages: English, Russian, Czech, Slovak (for 1st items French, too)

Social programme Inquiries: Tissue Bank, Faculty Hospital, 500 36 Hradec Králové, ČSSR.

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