

DELAYED REACTIVITY TO BACTERIAL AND VIRAL EXTRACTS IN THE AGED

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A number of reports have been published on decreased delayed-type reactivity in elderly persons to both contact allergens and bacterial/viral extracts. In the latter group reactivity to tuberculin was mostly studied. It has generally been stated that tuberculin reactivity is decreased in elderly persons (*e.g.* 3, 4). However, according to Waldorf *et al.* (13) there was no significant decrease in respect of tuberculin in their material, which included 104 patients between the ages of 59-99 years. Gervais *et al.* (3) found a decrease of the total reactivity in individuals over 80 years, compared with younger persons, if tested with tuberculin, candidin, microbial allergens, mold extracts and house-dust extract.

In elderly persons certain conditions may occur which are related to a delayed hyporeactivity. In this respect the lymphoma group is best known (*e.g.* 2, 5). But this phenomenon is also found in other types of cancer (7), especially among cancer patients in poor condition (5) although it is known that cancer tends to progress more rapidly in the fifth and sixth decades of life than in aged subjects (1). Other conditions, in which delayed hyporeactivity frequently occurs in the aged include rheumatoid arthritis and, according to a more recent report, uremia (10).

The aim of the present study was to investigate in an extensive material of elderly patients the delayed reactivity to a "bacter-

tery" of bacterial antigens as well as to a viral extract.

Material and Methods

Five categories of persons of both sexes were included in the study: Group I: 40 persons aged between 70-79 years; Group II: 40 persons aged between 80-89 years; Group III: 17 persons aged 90 years or over; Group IV: 20 persons aged 70-90 years, with diagnosed cancer (11 with prostatic, 6 with mammary, 2 with colonic and 1 with pulmonal cancer).

All these persons were patients in a geriatric clinic (Vårdhemmet, Stureby). Patients suffering from malignant lymphoma, rheumatoid arthritis or sarcoidosis were excluded.

The fifth group, the control group, consisted of 40 persons between 20-60 years of age, both inpatients and outpatients of a dermatologic clinic (Department of Dermatology, Karolinska sjukhuset, Stockholm). Cases of lymphoma, cancer, rheumatoid arthritis, sarcoidosis, and atopic dermatitis were excluded (for exclusion of the last-mentioned disease, see 8, 9).

The following test solutions were given intracutaneously to these persons (0.1 ml in the arms):

1. Tuberculin (National Swedish Bacteriological Laboratory) 0.1 mg.
2. Streptococcal extract.¹ The dose given

¹ Bencard, F. 1; Str. Pneumoniae type 1, Str Lancefield Group A, C, G, Str Salivarius.

- corresponded to 50 million organisms.
3. Combined staphylovaccine (National Swedish Bacteriological Laboratory). Polyvalent vaccine, prepared from heat-killed bacteria of about 12 hospital strains; several of these were of phage type 80-81. The dose given consisted of 0.15 U of alpha-toxoid and 6 million organisms. Merthiolate 0.01 % was added as a preservative.
 4. Mumps vaccine.²
 5. Schick test solution (National Swedish Bacteriological Laboratory).
 6. Schick control solution (National Swedish Bacteriological Laboratory).
- Physiological saline was used as control.

The delayed reactions were read at 24, 48 and, mostly, after 72 hours. Their grading was recorded as positive if the sum of the largest perpendicular diameters of the papule was more than 12 mm. In some cases biopsies were taken from reactions at 48 hours.

In Groups I-III the serum creatinine values were determined in all the patients.

Results

Delayed reactions occurred in Group I in about three-quarters of the patients; in the first place to staphylococcal extracts (in about half the total reactivity). The pattern was largely the same in Group II. However, in Group III, only one-quarter of the patients showed reactivity, and approximately 50 % in Group IV. The control group showed, with one exception, reactivity to the antigens used and to mumps vaccine.

Among the antigens the most frequent reactions observed were to the staphylococcal extract (in half the cases in Groups I and II) and, moreover, in about one-quarter of these Groups to mumps vaccine and to Schick toxin. There were very few reactions to the streptococcal extract and to tuberculin, whereas no reactions could be observed to the Schick control solution or to saline. Furthermore, many haemorrhagic

reactions were noted especially to the streptococcal extract (in Group II in nearly half the cases).

If the cancer patients were divided into two groups: those in good condition, and those in poor condition, then in the former, delayed reactivity was 9/11, haemorrhagic reactions occurred in 7/11, whereas 4/11 were negative. In the latter group the same ratios were 3/9, 6/9, and 4/9. There was no correlation between serum creatinine values and delayed reactivity.

Discussion

On the basis of the findings in the present study, there was no difference in delayed reactivity between age groups of the seventh and eight decades but, in this respect, there was substantial decrease in very old patients. The delayed reactivity was decreased even in the cancer patients, compared with that of the other investigated persons of the same age.

With regard to antigens there was a distinct difference between the frequent reactivity to the staphylococcal extract and the poor reactivity to streptococcal antigen (see below). The reactivity to mumps antigen and in the Schick test was parallel in Groups I or II. Mumps antigen was an obligatory elicitor of delayed reactivity in the control group. The poor reactivity to tuberculin was dependent on the relatively low concentration; in younger persons of the control group even the disappearance of reactivity after BCG vaccination may be relevant.

The high frequency of reactivity to pyococcal, mumps and diphtherial antigens in the control group, as well as their decreased occurrence in Groups I-IV are assumed to be due to the immune reaction acquired in earlier life, which subsequently decreases. A certain, primary toxic effect cannot be excluded, however, and the fact that patients in Groups II or IV reacted only to a lesser extent to the antigens used may signify a generally decreased reactivity to

² Lederle Laboratories.

Table 1. *Delayed reactivity of aged persons to i.c. bacterial and virus extracts*

	Delayed reactivity to						
	Tuberculin	Streptococc.	Staphylococc.	Mumps	Schick	Schick control	Negative
Group I: 40 pat. 70-79 years ¹	1	3	20	13	10	0	10
Group II: 40 pat. 80-89 years	0	3	20	10	10	0	11
Group III: 17 pat. 90 y. or more	0	1	2	4	1	0	13
Group IV: 20 cancer pat. 70-90	0	1	5	4	2	0	10
Controls: 40 pat. 20-60 years	8	23	34	39	21	0	10

¹ One patient may have several positive reactions.

Abbreviations: Streptococc. = Streptococcal extract (see methods)

Staphylococc. = Staphylococcal

Schick = Schick test solution

Table 2. *Haemorrhagic reactions in aged persons to i.c. bacterial and virus extracts*

	Haemorrhagic reactions to						
	Tuberculin	Streptococc.	Staphylococc.	Mumps	Schick	Schick control	Sum.
Group I ¹	0	9	0	1	0	1	11
Group II	0	17	0	2	3	4	26
Group III	0	10	0	3	0	3	16
Group IV	0	8	0	3	1	1	13
Controls	0	0	0	0	0	0	0

¹ One patient may have several reactions.

For abbreviations see Table 1.

both allergic and primary toxic stimuli. Especially mumps vaccine in the concentration used (undiluted), may have an irritant effect, although, on the other hand, approximately 80 per cent of an urban population has contracted the disease by the age of seventeen (15).

Haemorrhagic Reactions

The haemorrhagic reactions failed to occur in persons between 20-60 years of age and showed a straight increase with age; they occurred most regularly in very old persons. The pattern in cancer patients corresponded approximately to that in the higher age group (Group II). Most reactions were observed after the streptococcal extract. But there were also reactions to mumps, Schick control and Schick toxin. No such reactions were noted to staphylococcal extract or to

tuberculin. These reactions to staphylococcal extracts have already been described (10, 11). In this respect, the Schick control, *i.e.* heat-inactivated diphtheria toxin, had a more pronounced effect than the unactivated diphtheria toxin.

The microscopic investigation of the haemorrhagic reactions to streptococcal or other antigens showed—mostly but not always—extravascular erythrocyte cumulation along with signs of a pronounced perivascular inflammation, mainly of a vasculitis character. The picture was somewhat similar to the description of the haemorrhagic microbid reaction (6, 11, 12) (Figs. 1 and 2).

The evaluation of the haemorrhagic reactions is difficult. On the one hand, their correlation with age may correspond to the increased vascular permeability and fragility in senile purpura. On the other hand, the

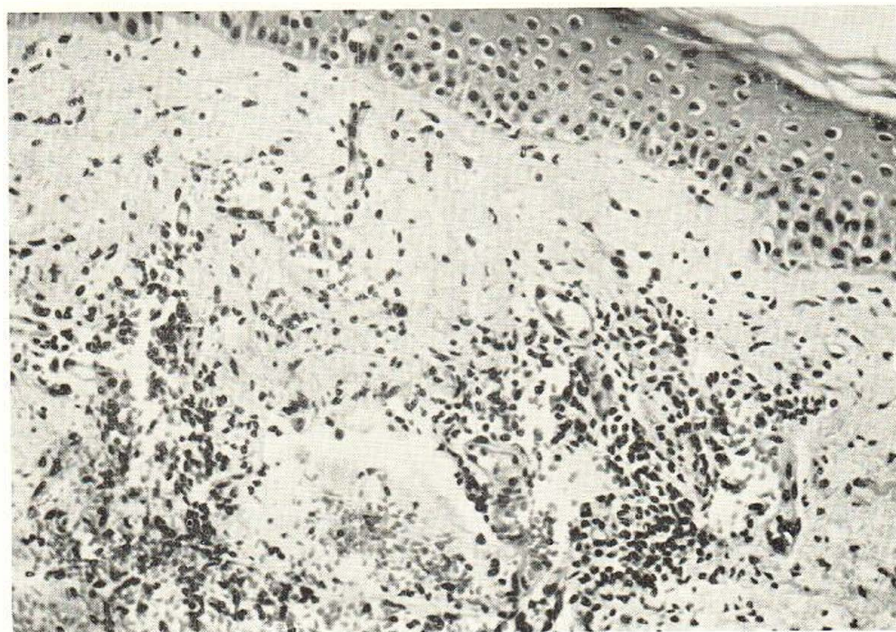


Fig. 1.

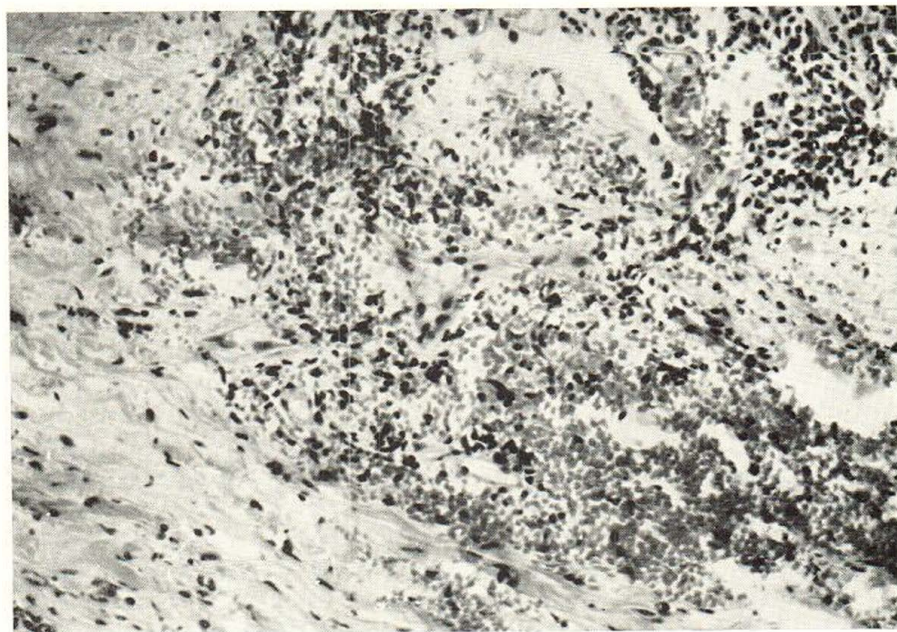


Fig. 2.

following features should be noted a) the histologic picture, b) the few delayed but very frequent haemorrhagic reactions to streptococcal extract in elderly persons which taken *together* were about equal to the delayed reactions to other antigens, c) the not infrequent petechial eruption in streptococcal infections (sepsis, scarlatina etc.), in parotitis and in diphtheria. Storck discussed the possibility of specific/un-specific mechanisms in this type of reaction (12).

The significant divergence in the type of delayed reactivity between staphylococcal and streptococcal extract is not entirely understood. Presumably it is not due to a principal difference in the reactivity to these bacteria in the age groups studied, but rather due to the presence or absence of antigens in the "antigen pool" used. This produces the special vascular effect (to decrease the source of failure, injections were given from the same bottle to both the elderly and the control patients). In view of the occurrence of frequent streptococcal haemorrhagic reactions in very old persons or in persons suffering from cancer, the present author does not consider the haemorrhagic reactions in the patients studied as a purely delayed reaction, but as a special type of delayed response with a complex mechanism, due in part to increased vascular permeability and fragility in the aged.

SUMMARY

The delayed reactivity of elderly persons to tuberculin 0.1 mg, streptococcal, staphylococcal, extracts, mumps vaccine, and Schick toxin was investigated. There was parallelism of reactivity in 40-40 patients aged between 70-79 and 80-89 years respectively. A decrease was observed in 17 patients aged 90 years and over as well as in 20 cancer patients as compared with 40 controls between 20-60 years. Most of the observed delayed reactions resulted from staphylococcal extract and mumps vaccine. The latter caused reactions in all but one individual in the control group. Haemorrhagic reactions, especially to streptococcal

extract, increased with increasing age. They showed microscopical signs of vasculitis and leucocytoclasia. These reactions are believed to be a special type of delayed response with a complex mechanism, due in part to increased vascular permeability and fragility in the aged.

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