

From the Medical Out-patients' Department, University of Copenhagen.  
Subdivision for Allergic Diseases (Egon Bruun, M.D.).

## SPECIFIC HYPOSENSITIZATION AS A LONG TERM TREATMENT OF BRONCHIAL ASTHMA<sup>1</sup>

By

EGON BRUUN

Since 1941, it has been attempted at the Allergy Clinic of the University of Copenhagen to make systematic examinations on the value of specific hyposensitization in asthma.

On purpose it was decided to treat all cases of asthma in which an allergic condition was considered the basic factor, with specific hyposensitization, and to use further only symptomatic treatment.

First, 239 patients were treated with one single series of hyposensitizing injections, lasting 2-3 months (1). The results are shown in table 1; 88 per cent were definitely improved, but the period of observation was only 6-12 months.

As might be expected, these good, immediate results were not lasting; the same patients and several additional cases were reexamined after a period of observation of about three years (E. Henriksen (3)), and the percentage of improvement dropped from 88 to 60 (table 2). However, several of these patients had been treated with repeated series of hyposensitization, and it seemed as if the results were improved, if the patients were treated repeatedly (table 3). This may indicate

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<sup>1</sup> Read before the 4th Congress of Internal Medicine, Madrid 1956.

that by a continuous treatment over a period of several years, the therapeutical results might be improved.

TABLE 1

*Results of a single series of specific hyposensitization in 239 asthmatics, period of observation: 6-12 months (Bruun, 1945).*

|                      | Number of patients | Per cent | Average duration of asthma |
|----------------------|--------------------|----------|----------------------------|
| Without symptoms ... | 50                 | 20.9     | 7.0 years                  |
| Improved .....       | 161                | 67.3     | 9.1 years                  |
| Unchanged .....      | 27                 | 11.2     | 11.6 years                 |
| Worse .....          | 1                  | 0.5      |                            |
| Total .....          | 239 patients       |          |                            |

TABLE 2

*Results of short term treatment with specific hyposensitization in 478 asthmatics, period of observation: 3 years (E. Henriksen, 1951).*

|                               | Number of patients | Per cent |
|-------------------------------|--------------------|----------|
| Without symptoms .....        | 36                 | 7.5 %    |
| Almost without symptoms ..... | 38                 | 7.9 %    |
| Improved .....                | 212                | 44.4 %   |
| Unchanged .....               | 108                | 22.6 %   |
| Worse .....                   | 51                 | 10.6 %   |
| Dead .....                    | 33                 | 6.9 %    |
| Total .....                   | 478 patients       |          |

TABLE 3

*Results of specific hyposensitization in relation to the number of series of injections (E. Henriksen, 1951).*

| Number of series of injections | Number of patients improved | Per cent |
|--------------------------------|-----------------------------|----------|
| 1                              | 146                         | 57.2 %   |
| 2                              | 69                          | 57.0 %   |
| 3                              | 38                          | 65.5 %   |
| 4                              | 21                          | 75.0 %   |
| 5 or more                      | 12                          | 75.0 %   |

On the basis of this observation, we started in 1950, a continuous form of specific hyposensitization, in the way that a continuation course of the strongest dose which the patients can tolerate, is given once every second or every third week for about three years. After three years of treatment, the injections are generally interrupted. Before discontinuing the treatment, two things are aimed at:

(1) the patient must have been free from asthma for at least a year,

(2) the intradermal reactions to the allergens in question should be definitely weaker than before the treatment.

If the patient has not been symptomfree for at least a year, and if the intradermal reactions are not diminished, the specific treatment should be continued.

A total of about 600 asthmatics are included in this experiment, and, in 1955 (2) at Utrecht, the effect of this long term treatment was demonstrated graphically in the first 10 patients of the material. Two of these diagrammes will illustrate the way in which we are working (diagramme I). From the first diagramme it will be seen that a patient with a

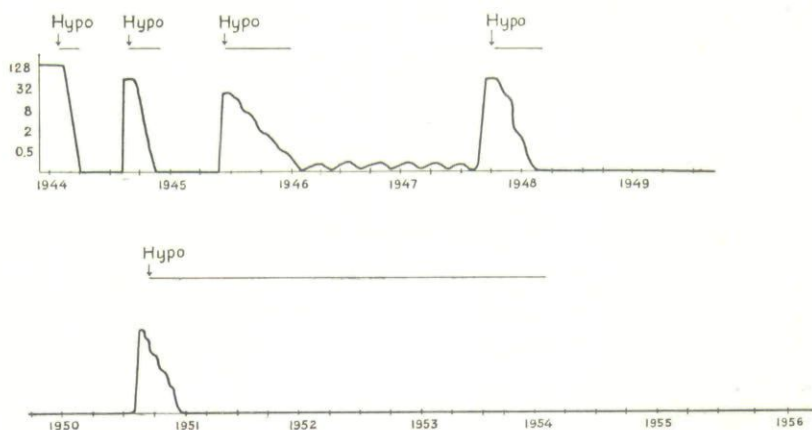


Diagramme I.

662/44 ♀ \*1890. Asthma since 1933. Allergic to house-dust. Ordinate: Average duration of asthma attacks (hours/month). Hypo = Specific Hyposensitization.

See the text, page 144-145.

severe bronchial asthma of a duration of 11 years can be greatly benefited by specific hyposensitization. It is seen, too, that the first attempts of hyposensitization (February to April 1944, September to December 1944, June to December 1945, and August 1947 to February 1948) all resulted in relatively short periods of relief, but sooner or later, she had relapses. When, in September 1950, the continuous form of hyposensitization was commenced, she obtained a permanent freedom from asthma, which has, till now, lasted for more than two years after discontinuance of the treatment. This is more than we had dared to hope for.

Another diagramme (diagramme 2) illustrates a case in which the result was unsatisfactory. In this case the curve never reaches the bottom-line, i.e. the patient never got free of symptoms; this patient is a baker, reacting allergically to flour, and it seems reasonable to consider the daily exposure to the specific allergen (flour) to be too intensive to obtain a good result with hyposensitization.

By means of such diagrammes it is possible to demonstrate the effect of specific hyposensitization as a long term treatment in asthma. Till now, 48 asthmatics, 24 male and 24 female, have been treated for at least three years and have been kept under observation for at least five years in all. 3 patients died (will be discussed later).

It appears that, after a period of observation of at least two

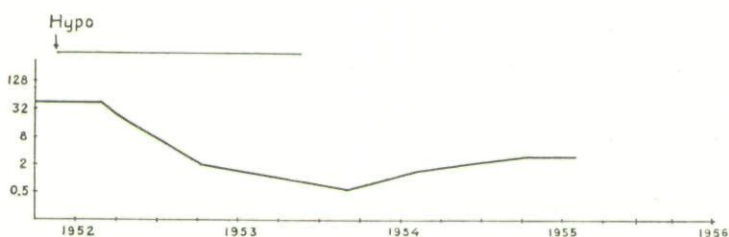


Diagramme 2.

3260/45 ♂ \*1925. Asthma since 1943. Allergic to flour (baker). Ordinate: Average duration of asthma attacks (hours/month). Hypo = Specific hyposensitization.

See the text, page 145.

TABLE 4  
*Specific Hyposensitization.*  
*Therapeutical results in 48 asthmatics.*

| Immediately after treatment                                      | After at least 2 years observation                                               |
|------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Symptom-free ..... 23                                            | Symptom-free ..... 16 }<br>Almost symptom-free ..... 2 } 23<br>Relapse ..... 5 } |
| Almost symptom-free ..... 13<br>(i.e. occasionally mild attacks) | Almost symptom-free ..... 10 }<br>Improved ..... 2 } 13<br>Relapse ..... 1 }     |
| Improved ..... 7<br>(i.e. > 50 % of improvement)                 | Improved ..... 6 }<br>Dead ..... 1 } 5                                           |
| Unchanged ..... 5                                                | Unchanged ..... 3 }<br>Dead ..... 2 } 7                                          |
| Total ..... 48                                                   | Total ..... 48                                                                   |

years after interruption of the specific hyposensitization, 16 patients were still free from asthma, and 12 almost without symptoms. Out of 6 patients who had had relapses, 4 were taken under treatment again with the result that now, three of them are without symptoms again, and one is almost free from symptoms. This means that by the end of the period of observation, a total of 19 were free from symptoms, and 13 were almost free from symptoms, 8 patients were improved, 5 unchanged or worse, and 3 had died.

Of the deaths, one patient had been treated for 18 months, but died in status asthmaticus; one discontinued the treatment by himself and died 6 months later, probably from a cancer of the lung (autopsy was not performed); finally one patient improved with specific hyposensitization, but wanted treatment with steroids, and died in status asthmaticus. It is generally agreed that about 5 per cent. of asthmatics sooner or later will die from asthma (Mc Cracken (5)). Already in 1944, Swedish authors (4) demonstrated a smaller mortality in specifically treated asthmatics than in controls, and dr. Hen-

TABLE 5

*Mortality rate in asthmatics treated with specific hyposensitization, and in asthmatics otherwise treated.*

|                               | Dead from asthma           |                  |
|-------------------------------|----------------------------|------------------|
|                               | Specific hyposensitization | Control material |
| Malmros & Rydberg, 1944 ..... | 1 %                        | 4 %              |
| E. Henriksen, 1951 .....      | 2.9 %                      | 4.9 %            |

TABLE 6

*Rate of invalide pension granted in specifically treated asthmatics, and in asthmatics otherwise treated (E. Henriksen, 1951).*

|                                  | Invalide pension granted on account of asthma |
|----------------------------------|-----------------------------------------------|
| Specific hyposensitization ..... | 1.9 %                                         |
| Control material .....           | 6.1 %                                         |

riksen, from the Copenhagen Clinic, made the same observation (table 5). The present material shows an asthma mortality rate of 4.1 per cent. This figure cannot confirm the above-mentioned good results; however, it must be pointed out that this relatively high mortality rate may be "bad luck", because, at present, the author is only aware of these two deaths from asthma in the whole material, comprising a total of about 600 patients. Final results on this point will be published later.

Another factor which must be taken into consideration, is the rate of invalide pensions granted to specifically treated asthmatics and to otherwise treated asthmatic patients. In Copenhagen, we found invalide pensions granted because of asthma in 1.9 per cent. in patients treated with specific hyposensitization, and in 6.1 per cent. in asthmatics otherwise treated (table 6).

On the basis of these observations it seems justified to recommend specific hyposensitization as a long term treatment in asthma. Whether three years of therapy is necessary, can-

not be decided yet; probably a more individual treatment should be aimed at on the basis of the strength of the intradermal reactions. Although there are exceptions, the general rule is a correlation between good results and definitely weakened, intradermal reactions. Therefore, it seems reasonable to continue the specific hyposensitization until the cutaneous reactions become definitely weaker than before treatment.

#### SUMMARY

Since 1941, it has been attempted at the Allergy Clinic of the University of Copenhagen to make systematic examinations on the value of specific hyposensitization in asthma.

On the basis of previously published results, we arrived at the conviction that specific hyposensitization should be continued for a long time, as a long term treatment, to obtain a good result. In 1950, a continuous form of treatment was started, in the way that a continuation course of the strongest dose which the patient can tolerate, is given once every second or every third week for about three years. After three years of treatment the injections are generally interrupted, and the patients are kept under observation in the following years.

A total of about 600 asthmatics are included in this experiment, and till now, 48 asthmatics have been treated for about three years and have been under observation for at least five years in all (i.e. at least two years after discontinuance of the specific hyposensitization).

By the end of the period of observation 19 patients were without symptoms, 13 almost without symptoms, and 8 were definitely improved, the percentage of improvement thus being 83.4 %. 5 patients (equal to 10.4 %) were not improved, and 3 had died, of these, 2 from asthma.

As a whole, the specific hyposensitization seems to offer the asthmatics a better future than other forms of treatment; an analysis of the specifically treated patients compared with control materials demonstrates that the mortality rate and

the rate of invalide pensions granted are both lower in specifically treated patients than in asthmatics otherwise treated.

## REFERENCES

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