

From Medical Department C, Københavns Amts Sygehus i Gentofte, Denmark  
(Copenhagen County Hospital). Head: M. Siggaard Andersen, M.D.

## TREATMENT OF BRONCHIAL ASTHMA WITH N-MUSTARD GAS

By

P. J. DRAGSTED & P. FROM HANSEN

Several observations suggest that N-mustard gas (erasol) exerts a certain anti-allergic effect. Inhibition of the Schwartzman phenomenon has thus been seen in rats after administration of N-mustard gas (3), and it has proved possible to cure immunization nephritis in rats with N-mustard gas (4, 5, 7).

In human pathology, too, N-mustard gas has been used in the treatment of nephritis, as it has been thought that this disorder involved an organo-allergic process of late onset.

However, this agent has exerted no convincing effect except in nephritis of a nephrotic nature.

In the nephrotic type of disseminated lupus erythematosus, N-mustard gas has also been used with good effect.

Further, From Hansen has treated cases of nephrosis in children with excellent effect in a few cases.

Several studies have been published on the administration of N-mustard gas to asthmatics (Jimenez Diaz (5)), who treated 17 asthmatics, and Arya (1), who treated a 17-year-old girl).

Both of these authors observed improvement, both subjectively and objectively, within the first 24 hours.

It has not been possible to estimate from these publications the effect on the eosinophils.

### WRITERS' INVESTIGATIONS

The purpose of the present study was to examine the effect of N-mustard gas on bronchial asthma, and eosinophilia; con-

sequently, the series of cases was selected so that all the patients treated presented pronounced eosinophilia.

The series comprises 2 males and 5 females aged from 20 to 40 years.

Before the examination, cutaneous tests and blood examinations were made in all patients, and all showed pronounced eosinophilia. Positive skin reactions, namely for tree pollen, were found in only one case, but the patient had never noticed any seasonal variation, and her primary attack had begun in the autumn.

N-mustard gas in the form of the preparation erasol was administered intravenously with saline solution. The single dose was 0.1 mg/kg, and this was administered on four consecutive days, so that the total dose was from 16 to 24 mg.

After treatment, leucocytes and eosinophils were counted, and the clinical condition of the patients was followed for a prolonged period (up to several years).

Except for the immediate effect of the treatment in the form of vomiting, all patients tolerated the treatment well; a few single doses of largactil were given, and the transient leukopenia caused no trouble.

TABLE I

*The results of counting the leucocytes and the eosinophils before and after treatment with nitrogen-mustard.*

| Name | Leucocytes |       | Reduction<br>in % | Eosinophils |       | Reduction<br>in % | Leucocytes +<br>eosinophils |       | Reduction<br>in % | Clinical<br>effect                |
|------|------------|-------|-------------------|-------------|-------|-------------------|-----------------------------|-------|-------------------|-----------------------------------|
|      | before     | after |                   | before      | after |                   | before                      | after |                   |                                   |
| K    | 7,000      | 3,000 | 60                | 1,500       | 300   | 80                | 5,500                       | 2,700 | 50                | good                              |
| W    | 9,000      | 6,000 | 33                | 4,000       | 500   | 88                | 5,000                       | 5,500 | 0                 | good                              |
| S    | 8,000      | 4,000 | 50                | 1,300       | 500   | 62                | 6,700                       | 3,500 | 48                | unsatis-<br>factory               |
| G    | 9,200      | 6,500 | 30                | 1,800       | 500   | 72                | 7,400                       | 6,000 | 19                | good                              |
| C    | 9,500      | 7,00  | 26                | 3,000       | 1,250 | 58                | 6,500                       | 5,750 | 12                | no data                           |
| J.P. | 12,000     |       |                   | 8,000       |       |                   | 4,000                       |       |                   | available<br>allergic<br>reaction |

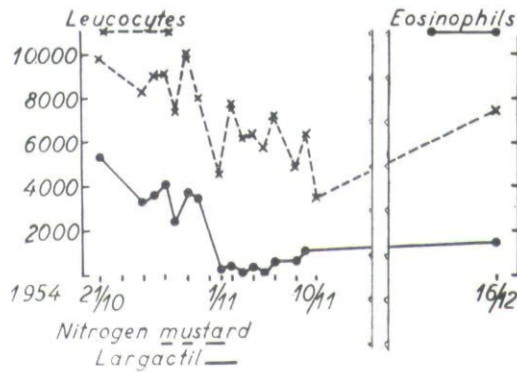


Fig. 1.

Fig. 1 shows the decline in the number of leucocytes and eosinophils following infusion of nitrogen mustard.

Table I shows the changes observed in the patients treated. The fall in the total number of leucocytes was about 40 per cent, the eosinophils showed a fall of 72 per cent, whereas that of the other cells averaged only 26 per cent.

In two patients, daily counts of the number of segments in 100 eosinophils were made. This examination showed that in the days following the administration of N-mustard gas cells with a low number of segments, presumably the most unripe cells, decreased most in number.

The last patient completed the treatment, but has not been followed.

The curve in Figure 1 shows a typical course of the number of eosinophils and leucocytes after treatment with N-mustard gas.

The series was followed up in 1957. One patient had died (in Hamburg) in status asthmaticus. One patient lives in Iceland, and one had been admitted to a home, as she was disabled by pulmonary fibrosis. The other four patients were doing fairly well, but were not free from asthma. They had normal leucocyte figures.

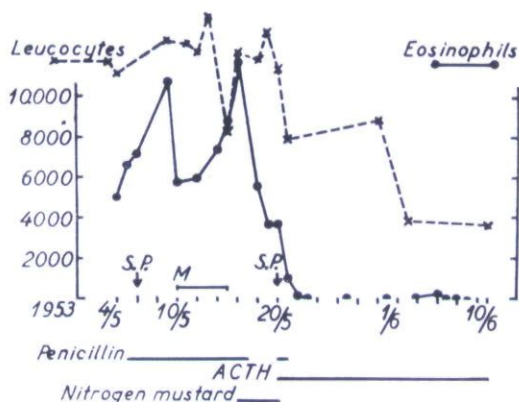


Fig. 2.

The decrease in leucocytes and eosinophils in the patient who developed shock (21/5). S.P. = sternal puncture. M = menstrual period.

#### DISCUSSION

As shown in Table I, three patients obtained a striking improvement. This began on the third day in all; the patients said that the oppression disappeared, and that their breathing was unimpaired. This could be confirmed by physical examination, as no râles were heard on auscultation, and respiration became deeper and without wheezing.

This improvement began simultaneously with an appreciable fall in the number of eosinophils.

The day when the improvement began is against the possibility of a psychogenic improvement. In our opinion the unpleasant, immediate side-effects would make the patients declare either that they were satisfied at once or that they had improved when they knew that the treatment had been finished.

Nevertheless we do not feel quite convinced that there is a connection between the number of eosinophils in the blood and the clinical improvement of the condition. It may thus be mentioned that a great number of eosinophils in the sputum both before and after treatment remained unchanged. Also, one patient developed a constitutional reaction in connection with

the treatment at a time when the number of eosinophils was falling, though still increased.

The curve in Figure 2 shows the course in this patient.

Owing to the presence of pneumococci in the sputum the patient was given 300,000 units of penicillin daily for a fortnight. The number of eosinophils during this period was about 10,000. When the pneumococci had disappeared but the asthma was still pronounced, it was decided to treat the patient with N-mustard gas. On the last day of this treatment the number of eosinophils had fallen to 4,000. To prevent another bacterial attack on the bronchi during a period of possible leucopenia, it was decided to give another course of treatment with penicillin, this time with 2 million units of Na-penicillin daily. The patient had barely received the first dose when he developed a violent anaphylactic reaction, which was only overcome by epinephrine, hydrocortisate and ACTH.

The reason why the patient developed a constitutional reaction may be the large single dose of penicillin after prolonged treatment and a few day's pause (the patient had previously received penicillin without developing any shock). The time when the reaction occurred may possibly be explained by (1) still existing large numbers of eosinophils, (2) increased amounts of H substance (released substance) owing to degeneration of eosinophils.

The eosinopenia obtained may be indicative of a reduction of the allergic condition, or may be due to greater vulnerability of the eosinophils and/or their precursors but without any change in the allergic condition.

#### CONCLUSION

(1) In bronchial asthma with pronounced eosinophils, N-mustard gas produces an elective reduction in the number of eosinophils. (2) In a few patients a striking, though temporary, improvement was obtained, without any definite improvement of the long-term prognosis. (3) N-mustard gas may be indicated in protracted, resistant asthma with eosinophilia,

especially in the case of dangerous attacks and when other more specific anti-allergic treatment has been attempted without success.

#### SUMMARY

Seven patients with bronchial asthma and pronounced eosinophilia have been treated with N-mustard gas. This resulted in a fall in the number of eosinophils which was more pronounced than in the case of the other white cells.

The Schilling index suggested that the most unripe (or least segmented) cells were most vigorously destroyed. At the time when the number of eosinophils decreased in the blood, three of the patients showed a pronounced improvement.

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