

NETHERLANDS ASSOCIATION OF ALLERGY

LECTURE - DEMONSTRATION - EVENING

January 25th 1952

W. J. Quarles van Ufford, of *Utrecht*, demonstrated some patients with bronchial asthma showing unusual changes: an infant with an enlarged thymus, a young man who was extremely hypersensitive to house dust, but he, for the past year, had only been subject to attacks after violent quarrels with his father (he was strongly attached to his mother), and a boy who twice had a left-sided spontaneous pneumothorax in the course of 3 years, in whom a lipiodol examination failed on two occasions, as the lipiodol did not continue on its course in spite of previously taken measures, which was subsequently found to have been due to a spasm, and in whom no cysts etc. were observed.

Secondly the allergic manifestations of the large intestine was discussed, particular attention being drawn to the important symptom of shifts in an otherwise non-pathogenic intestinal flora. The fact that there are numerous possible symptoms, the necessity of a thorough clinical (and X-ray) examination in order to eliminate other causes, the frequent absence of definite allergic manifestations (history of the patient's family, eosinophilia, skin diseases, etc.) and the value of an elimination diet were stressed.

Some patients were discussed.

LECTURE - DEMONSTRATION - EVENING

March 13th 1952

H. van Marken Lichtenbelt (Zeist) demonstrated some patients with pathological changes of the tongue, in one of which treatment with antihistaminics resulted in the disappearance of the lesions.

The question was put as to whether a food allergy may manifest itself solely in changes of the tongue (swelling, furred tongue).

Finally, the case of a patient with periarteritis nodosa, in which the diagnosis could be established during life, was discussed. X-ray pictures of the thorax and photographs of morbid anatomical findings were presented.

The marked variation of colic-like pains and the absence of asthmatic manifestations (although a bronchopneumonia was present in this case) were stressed. The differential diagnosis (generalized necrosing arteritis, endarteritis obliterans, vascular changes in rheumatism) was discussed.

Attention was drawn to the danger of using sulphonamides in this disease.

THIRD GENERAL SCIENTIFIC MEETING

Leiden, March 22nd 1952

Chairman: *W. Kremer, M.D.*

CHANGES OF THE LUNGS AND THYMUS AND BRONCHIAL ASTHMA by W. J. QUARLES VAN UFFORD, M.D.

A statistical review of the findings in X-ray examinations (D. S. Bartstra, M.D.) in 700 patients with bronchial asthma.

No changes	214 (30.57 %)	
Slightly increased hilar shadow.....	138 (19.71 %)	—343 (49 %)
Considerably increased hilar shadow	205 (29.29 %)	
Streakly pulmonary shadow	91 (13.00 %)	
Left pleural sinus fails to expand ...	4 (0.57 %)	
Moderately movable diaphragm ...	175 (25.00 %)	—288 (41.14 %)
Barely movable diaphragm	113 (16.14 %)	
Suspicion of tuberculosis	7 (1.00 %)	
Spots (bronchopneumonic etc.)	15 (2.14 %)	
Pulmonary abscess	1 (0.14 %)	
Suspicion of pulmonary cysts	3 (0.43 %)	
Enlargement of the left heart	27 (3.86 %)	
Pneumothorax	2 (0.28 %)	
Silicosis	2 (0.28 %)	
Siderosis	1 (0.14 %)	

In view of this low incidence of severe complications it is believed that there is no point in carrying out a complete examination of the lungs as a routine procedure in patients with bronchial asthma, although in practice the objections made by Gay et al. (hypersensitiveness to iodine—which may, however, be eliminated by a preliminary potassium iodide test—resulting in a non-specific pneumonia) are less serious than might be anticipated.

Thereupon some patients, in whom changes had been found, were described:

In 1951 five infants (with a family history of asthma) were seen, with asthmatic complaints, which had practically been present since birth and started after the catching of a cold. X-ray examination revealed an enlarged thymus. Some cases were treated with roentgen irradiation, in others with an only slightly enlarged thymus the result of a course of treatment with autovaccine was awaited. The rule, given inter al. by *Cooke*, not to make tests for hypersensitivity before the thymus has grown smaller, as otherwise a constitutional reaction may be liable to increase the danger of a status lymphaticus, was adhered to.

Hajos states that the thymus promotes the symptoms of anaphylaxis and idiosyncrasy. While X-ray therapy will suffice in otherwise normal children, preventive measures (inoculation against whooping cough, cold ablutions, dietary measures, etc.) are advisable in these children. Photographic plates were demonstrated.

Pulmonary changes mainly consist in chronic bronchitis, bronchiectasis, silicosis etc., tuberculosis, sarcoid of *Boeck*, cysts and abscesses (case reports, with photographs).

The problem of chronic bronchitis is a difficult one: in some cases it is primary, in others secondary, but even then it occasionally constitutes one of the aetiological factors. The fact is stressed that a diagnosis of chronic bronchitis should indeed be based upon other manifestations than mere coughing and expectoration of sputum. Exacerbations, temperature, erythrocyte sedimentation rate, presence of leukocytes in the sputum, etc. should be noted.

The principal changes in bronchial asthma reported in the literature are cylindrical bronchiectases (*Derbes Engelhardt, Chapman Hoskins, Cooke, Feinberg, Tuft*), while the comparatively small incidence (*Bullen*, 7.75 %), especially when associated with inflammations of the paranasal sinuses, is emphasized. In 50 cases of asthma *Wiswanathan* observed 14 patients with bronchiectasis, 6 of which

showed a sacculated and 5 a cylindrical bronchiectasis. *Watson* and *Kibler* found 90 % of their patients with bronchiectasis to be allergic. The result of surgical treatment is extremely doubtful. In one patient with asthma and bronchiectasis the complaints increased to such an extent after operation, that he died rapidly. In addition a little patient with asthma, in whom a maxillary sinusitis was associated with bronchiectasis and numerous pathological changes (including clubbed fingers), was described; in this case surgical treatment was impossible owing to the extent of the lesions and chemotherapy as a last resort failed.

It is true that one female patient could be kept in balance with an autovaccine and chemotherapy after operation had failed to produce results. In this case the bronchiectases obscured and dominated the clinical picture of bronchial asthma, but the attacks of dyspnoea were also able to increase owing to the bacterial insusceptibility. Measures against the bacterial, inhalation and dietary factors continued to be necessary and occasionally they afforded a temporary relief.

Complaints of silicosis frequently start to appear following the development of a bronchitis. Some patients with silicosis, who had been sent for examination with a clinical picture of bronchial asthma, were reviewed. In some of these cases there were allergic factors, treatment of which occasionally resulted in the disappearance of the attacks of dyspnoea. In a hearth-polisher (contact with emery) the violent attacks of dyspnoea occurring during a status asthmaticus could be treated successfully, although a feeling of oppression persisted. Work in the open air was prescribed in this case.

Actually the relationship between tuberculosis and asthma is a problem requiring separate discussion. Glands (*Cooke*), fibrosis or strictures may give rise to asthma-like attacks. In *Tuft's* opinion there is no relationship between asthma and tuberculosis, according to *Feinberg* pulmonary tuberculosis is less frequent in cases of asthma. *Cantonnet* believes tuberculosis to constitute an aetiological factor in asthma.

There are three possibilities: 1. Having had a tuberculosis may promote the onset of allergic symptoms (allergic diseases frequently appear after some form of infectious disease). 2. Hypersensitivity to tuberculin. 3. A complicating chronic bronchitis may result in bacterial allergy.

When the erythrocyte sedimentation rate continues to show an increase which cannot be explained, one must persist in looking for tuberculosis, even when the initial results have been negative.

Finally the lecturer described some patients with pulmonary cysts and pulmonary abscesses. The latter were characterized by the striking fact that during the presence of the abscess, which was accompanied with fever and frequent expectorations, the patient was not troubled by her asthma. Chemotherapy resulted in the disappearance of the abscess, the violent attacks of dyspnoea requiring a separate and prolonged treatment.

If the above-mentioned changes are to be held to play a primary rôle with regard to bronchial asthma, there must be a bacterial allergy. Otherwise these changes may be an incidental disease aggravating the symptoms or obscuring the clinical picture, or they merely are an accidental finding causing no or entirely separate manifestations. But in the event of particular findings during the examination for allergy (such as a markedly increased erythrocyte sedimentation rate, dyspnoea only during exercise, expectoration of large quantities of sputum, complaints of excessive fatigue) one should guard against overlooking a tuberculosis or other pulmonary changes. In that case a general examination is indicated.

LYMPHATIC TISSUE AND THE MECHANISM OF ANTIBODY PRODUCTION *by C. BELONJE*

OBSERVATIONS REGARDING THE SENDING OF CHILDREN TO THE SEASIDE FOR ASTHMATIC BRONCHITIS *by G. BELONJE*

The investigation could be divided into two parts. In the first part studies were undertaken to determine the extent to which the changes, shown initially by the children, had improved as a result of treatment at the colony, while the second part dealt with the question as to whether a possible correlation might be shown to exist between the onset of an attack of bronchial asthma and meteorological phenomena.

In behalf of the former investigation the case histories from the period 1945-1949 of 5 different colonies were studied, those charts being removed which referred to patients with asthma.

Attempts were made to unravel this tangle of possible effects by using some modern methods of statistical analysis, by occasionally calculating the "confidence interval" and the chance of improvement, by employing the g^2 test and by variation analysis.

The following method was used to compile the tables and make the calculations. A moderate improvement was qualified as O. Only the

number of O and V of a single stay were taken into account, in order to make the comparison as honest as possible. The periods of stay were divided into spring, summer, autumn and winter, according to the customary climatological method, which is: Sp. = March 1st–June 1st; S = June 1st–Sept. 1st; A. = Sept. 1st–Dec. 1st; and W. = Dec. 1st–March 1st. The period of stay was regarded as belonging to that season, during which it mainly occurred.

CONCLUSIONS

1. Sex had no effect on the chance of improvement.
2. There was no significant difference between the age groups of 6–8, 9–11 and 12–14.
3. There was a marked and significant difference between the various seasons. The greatest number of improvements was observed in the autumn, followed by W., Sp. and S. respectively.
4. There was no difference between the results in large, medium-sized and small colonies.

This investigation was carried out in 5 so-called A colony-homes. It showed that the number of improvements in A colonyhomes was greater than that in the seaside home; this is understandable, as only the milder cases are admitted to the A colony-homes. Likewise the number of improvements—though only those which had occurred during a period of one year—in the seaside home were studied and compared with the number of improvements shown by these same children, after they had returned to their families for at least half a year. The following results were found:

	Boys	Girls	Total
On leaving	68.5	81.8	71.7
Later on	35.2	44.4	37.8

From another convalescent home, not by the sea, the lecturer later also learnt the number of improvements for asthma. For boys and girls together it proved to be 36 %. This result is particularly remarkable owing to the fact that this improvement rate, compared with the values found by *Verschoor*, a colony physician in another convalescent home not situated by sea, showed a significantly greater number of improvements. Subsequent investigation, continued for a considerable number of years, will have to show whether this is a constant occurrence. But

in that event the fact should be noted whether a severe or more mild case of asthma is involved!

I still wish to draw attention to one detail, which was noticeable during the examination of patients with asthma. For it appeared that those children who had gained most in weight showed the least improvement.

Second part of the investigation.

As occasional publications had drawn his attention to the relationship between a meteorological phenomenon and attacks of asthmatic bronchitis, the lecturer decided to investigate this matter. The colonies seemed particularly suitable for this purpose, as:

1. the children live under identical conditions,
2. without, or practically without, contact with the neighbouring population,
3. enjoy good hygienic care, while
4. accurate and detailed observations can be made, and finally
5. as the children receiving attendance are usually weak, so that they will rapidly respond to various noxae, especially in the beginning of treatment.

The problem was whether there was a correlation between a meteorological phenomenon and an attack of bronchial asthma.

To study this problem it was essential to obtain the following data:

1. The dates on which attacks of asthma occurred in a colony.
2. Meteorological data, recorded in situ or in the immediate vicinity of the colony. When these were not available or were not regarded as essential for meteorological reasons, then data referring to the entire country were considered to be sufficient.

The dates mentioned under 1 were recorded for at least a year in 5 different colonies, the data mentioned sub 2 were supplied by the Director of the Department of Climatology of the K.N.M.I. (Royal Meteorological Office of the Netherlands) in de Bilt, while part of these data resulted from personal observations and others from subsequently verified information supplied by the matron of a colony of the "Centraal Genootschap", who was able to make the observations thanks to the willingness of the board to allow a meteorological observation post to be placed on the grounds of the colony.

For various reasons the dates on which attacks of asthma occurred could not be compared with solar flames, sun spots, cosmic radiation and atmospheric electricity. For the first three are too incomplete or

too small in number to be able to coincide with the numerous attacks of asthma, while the potential difference varies too frequently and too widely.

Statistically the dates on which the attacks of asthma occurred were, however, compared with:

1. Front passages.
2. Days on which the magnetic field was slightly and considerably disturbed.
3. Days of east wind (in which the east component occurs).
4. Days on which humidity was high and very high.

Reports on these data showed that:

1. Small numbers of asthma-free days between 2 successive days on which attacks of asthma occur are more frequent than the number which may be attributed to chance.
2. Days with frequent attacks of asthma occur more often than may be ascribed to chance.
3. Attacks coinciding with days on which a front passed, are purely accidental.
4. Attacks coinciding with days on which the magnetic field was disturbed are purely accidental.
5. The same applies to days on which the magnetic field was considerably disturbed.

Further there was no reason for assuming a relationship between a day on which attacks of asthma occurred and a day of east wind. This refers to the claim of certain investigators that the number of attacks of asthma at the seaside increases considerably when an east wind is blowing. The data obtained by the lecturer,—in which an east-wind day was assumed to be a day on which the wind direction had an east component in at least 2 out of 3 observations—are in no way suggestive of this fact.

Finally a comparison was made with days on which humidity was high and very high. Though a slight relationship was found between attacks of asthma and a high degree of humidity (mean relative humidity over 80 %), this relationship decreased to an even further extent when a comparison was made with days on which humidity was extremely high (mean relative humidity over 90 %). Accordingly no definite relationship could be demonstrated.

Therefore this investigation has not shown—as many believe with-

out conclusive evidence—that there is any definite relationship between the recorded attacks of asthma and the meteorological observations studied.

With regard to treatment it is assumed to be of importance to send out children, affected to a more or less severe degree, preferably to a district or place where they may work and learn like ordinary children, but where mental stimuli can be avoided and the atmosphere is not charged with industrial air pollutions and secondary infections can be prevented as much as possible.

The stay at the colony should depend upon the severity of the condition, while corrective measures should also be taken in the domestic surroundings of the child (inter al. to resolve a possible mental discord, but also to guard against excessive care!).

Finally, a sufficient number of improvements, amounting to approximately 36 %, persisting for at least half a year after the child has been sent to the colony, does suggest that positive results may be obtained by this method, although it will undoubtedly be possible in certain cases to improve or bring about the disappearance of the disease in severe patients by other procedures or even without any demonstrable therapy.

The lecturer is inclined to believe that a prolonged stay in the colony will increase the child's resistance, both to mental and physical stimuli (the allergic response possibly diminishing as a result), so that it may be possible "to help the children through a difficult period" and, in some cases, to bring about a permanent recovery by sending them out.

SALVARSDERMATITIS *by* J. P. E. BURBACH (published N. T. v. G.)

A COMPARISON BETWEEN SKINTEST AND INHALATIONTEST *by*
H. J. TEN CATE (published N. T. v. G.)

LECTURE – EVENING

Amsterdam, May 1st 1952

FOOD-ALLERGY *by* Dr. W. KREMER

The difference between intracutaneous and scratch-tests for food-allergy is discussed. In the opinion of the speaker the first are much more preferable and trustworthy. This is elucidated with different

facts from literature and from own experience. He tells about some cases in which after abstinence of the food, for which the patient was hypersensitive, the hyper-sensitiveness disappeared within about half a year.

In the meantime the patient had sensitized himself against new foodstuffs of which he had made use during this time. So in many cases it is most probable, that when a skin-reaction for a certain food is positive or weak-positive, either the patient is going to become more and more hyper-sensitive to this food or the reverse, depending on the use or obstination of that food. Therefore weak skin-reactions should not be neglected in the prescription of an allergen-free diet.

LECTURE – DEMONSTRATION – EVENING

Doorn, Tuesday July 8th

H. P. Lansberg (Zeist) demonstrated a patient with a violent allergic eczema of both hands, which had been treated by various methods, only lentil baths having afforded a temporary relief. On treatment with wet compresses of (3.8 %) sodium citrate for 14 days, the eczema had practically disappeared. To prevent secondary infections the patient was treated with injections of staphylococcus toxoid (R.I.V.).

K. Magnus (Doorn) presented a preliminary report on his work (in co-operation with *H. P. Lansberg*) regarding serological tests in tuberculosis (Dubos-Middlebrook technique). Tests were made by neutralizing the serum with tuberculin at various dilutions; the titre and skin responses were compared.

4TH SCIENTIFIC MEETING ON NOVEMBER 22ND 1952

in the lecture-room of Prof. Prakken in Amsterdam, and continued on December 20th 1952 in the Laboratory of Hygiene in Utrecht.

Chairman: *W. Kremer*, M.D.

Th. Strengers, M.D.: Determination of the problems and scheme of work of the histamine research team.

Prof. J. Hemelrijk: Statistics and medicine.

J. A. H. Gooszen, M.D.: Changes in the histamine level during work.

Th. Strengers, Ch.D.: The combining of tissue with histamine.

J. Verschure, M.D.: Reactions of the tissue histamine in anaphylactic shock.

Miss *J. Maas*: Variations in the histamine level of the blood in normal, allergic and tuberculous children.

P. Sjoukes: Histamine and the adrenals.

J. Verschure, M.D.: The biological relationship between adrenalin and histamine.

(These papers will probably be published together as a supplement of *Acta Allergologica*).

TREATMENT OF BRONCHIAL ASTHMA WITH CORTISONE by W. J. QUARLES VAN UFFORD

Personal indications.

1. cortisone in attacks of asthma
2. " " status asthmaticus
3. " " seasonal asthma
4. " " chronic asthma
5. " " " " after preliminary treatment with ACTH.

Some cases were discussed:

Sub 1. Injections of cortisone alone, or in combination with adrenalin, produced no better results than injections of adrenalin (or even failed).

Sub 2. In 2 cases the desired results was obtained with injections of cortisone.

Sub 3. A course of treatment with cortisone tablets (in decreasing dosage), given in 3 cases (July–September bronchial asthma), was completely successful in 2 cases and fairly successful in 1 case.

Sub 4. Three patients received a course of treatment with cortisone tablets, the result being highly favourable in 1 and moderately favourable in 1 case, while treatment failed in 1 case.

Sub 5. Four extremely severe cases were initially treated with intravenous injections of ACTH (cortrophin), cortisone tablets being administered once the patients were free of complaints. Cortisone was administered in decreasing doses for 6 weeks (1/4th tablet, 6 mg., daily during the last week), whereupon ACTH was given by intravenous drip for 1 day, followed by another 6 weeks of treatment with cortisone, etc.

In 2 cases a satisfactory and in 2 others a reasonably satisfactory result was obtained.

THE PREVENTION OF COMPLICATIONS RESULTING FROM INTRA-BRONCHIAL EXAMINATIONS *by* K. MAGNUS

1) The dangers of bronchography, bronchoscopy and bronchosprometry are very slight, provided the directions are complied with and the necessary patience, skill and experience are available.

2) The greater danger consists in hypersensitiveness to pantocaine. Fatal complications may frequently be prevented by the immediate intravenous injection of pentothal or kemithal.

3) When an intrabronchial examination is followed by the appearance of a status asthmaticus, which fails to respond to the usual methods of treatment, one should not hesitate to administer ACTH.

ALLERGY *by* Prof. K. C. WINKLER

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