

PROCEEDINGS

COMMUNICATIONS

GESELLSCHAFTSVERHANDLUNGEN

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NETHERLANDS SOCIETY OF ALLERGY

*Meeting, May 16th, Groningen*

Chairman: Dr. Willem Kremer

Elected as Honorary Members:

Dr. *F. W. Wittich*, Minneapolis,

Dr. *E. B. Salén*, Stockholm.

SOME FINDINGS REGARDING THE EFFECT OF PREGNANCY  
ON ALLERGIC DISEASES

(From the Department of Allergy, Diaconessenhuis, Utrecht)

*W. J. Quarles van Ufford*: Pregnancy plays an important part in the lives of women. The wife of one of my acquaintances only saw her gallbladder disturbances disappear during pregnancy; another continued to be weak and ill until after the birth of her first child. Does this suggest a shift in the balance between the vagus and sympathetic nervous system in favour of the latter?

Pregnancy is also seen to have a marked effect on the lives of our asthmatic patients. A patient with asthma told me that, among other things, her ten children had been born so soon after one another, because she felt so well during these periods. In another patient the oviducts were ligated some weeks previously at the request of her family practitioner, as violent attacks of asthma occurred during and after every pregnancy.

In this paper attention is paid to four findings:

1. The very constant finding that attacks of asthma etc. increase during the first period of pregnancy and subsequently decrease.

2. The appearance of urticaria during the first months of pregnancy. (Allergic explanations of vomiting of pregnancy and the like are not discussed in this paper).

3. The appearance of allergic reactions almost immediately after labour.

4. The disappearance of allergic reactions after labour.

Apparently sex hormones play an important part in allergic reactions. Asthma is claimed to be liable to aggravation just before the menarche and to disappear after it (table 1).

TABLE 1.

*Menarche and allergic diseases.*

Studied 100 cases (girls 11-14) (bronchial asthma).

|                         |    |
|-------------------------|----|
| Worse before .....      | 18 |
| „ after .....           | 1  |
| Disappeared after ..... | 1  |

TABLE 2.

*Allergic diseases starting after menarche.*

|                            |                          |
|----------------------------|--------------------------|
| Bronchial asthma .....     | 15 % (studied 500 cases) |
| Hayfever .....             | 31 % ( „ 50 „ )          |
| Rhinitis vasomotoria ..... | 18 % ( „ 60 „ )          |
| Urticaria .....            | 11 % ( „ 65 „ )          |

Hay fever and vasomotor rhinitis as well as asthma and urticaria frequently first appear at the age of sexual maturity (table 2). Patients with asthma are often apprehensive of the days prior to menstruation (table 3). The disturbances are stated to subside and even the skin tests are claimed to be only slightly positive or even negative after the onset of menstruation. The climacteric is frequently announced to coincide with the disappearance of the allergic reactions, while, on the other hand, symptoms of bronchitis may start to appear at this time (table 4).

Much has been written about the effect of pregnancy. According to Kolmer and Tuft the tuberculin test becomes less marked during pregnancy, Lichtenstein observed a decrease in 25 % of the cases during the last 3 months, Ahlmark found an increased histaminase activity of the blood during the 7th week, which subsequently showed a further

TABLE 3.  
*Menstruation and bronchial asthma.*  
Studied 100 cases.

|                    |    |                     |   |
|--------------------|----|---------------------|---|
| Worse before ..... | 28 | Better before ..... | - |
| „ during .....     | 4  | „ during .....      | 2 |
| „ after .....      | 1  | „ after .....       | 2 |

No difference 61 (in rhinitis vasomotoria 81 %).

2 cases complaining only of bronchial asthma during the menstrual period (both strong hypersensitive to house-dust) and one to milk.

In 7 of 100 cases complaints about irregular menstruation.

TABLE 4.  
*Climacterium and allergic diseases.*  
Studied 100 cases.

| Bronch. asthma      |      | Hayfever | Rhinit. vasom. | Urticaria |
|---------------------|------|----------|----------------|-----------|
| Better .....        | 3 %  | 16 %     | 12 %           | -         |
| No difference ..... | 85 % | 83 %     | 84 %           | 87 %      |
| Worse .....         | 2 %  | -        | -              | 3 %       |
| Started .....       | 10 % | 1 %      | 4 %            | 10 %      |

increase, Solomonica and Kurzrok showed that an extract of urine of pregnancy inhibited the anaphylactic reaction of guinea-pigs to horse serum; Feinberg attributes the favourable condition to an effect on the nervous system and metabolism as a whole, or to a simple direct action; Ratner, however, states that it is generally believed that women do not lose their serum hypersensitiveness during pregnancy. On the other hand is the asthma of pregnancy; de Gennes and Mahoudeau assert that asthma of pregnancy mainly occurs during the 4th-6th month, a period during which the activity of the oestrogens and progesterone shows a considerable increase; Naegeli has drawn attention to the possibility of allergic reactions occurring when antibodies of the foetus and mother reach each other too soon. Urbach and Gottlieb also believe it to be probable that allergic reactions during pregnancy are due to an excessive susceptibility to placental or foetal proteins. Finch assumes the hypersensitive reaction of pregnancy to be a hypersensitiveness to progestin and administered 10 ml. of normal pregnancy serum twice weekly, while Putzy Doneddu gave lutein and an extract of the anterior lobe of the pituitary. Cooke explains allergic

TABLE 5.  
*Pregnancy and allergy.*

Studied 50 bronchial asthmatic cases, 10 hayfever, 10 rhinitis vasomot.,  
10 urticaria, 10 allergic eczema.

|                                             | asthma | hayfever | rhinitis | urtic. | eczema |
|---------------------------------------------|--------|----------|----------|--------|--------|
| No change .....                             | 10 %   | 90 %     | 80 %     | —      | 10 %   |
| Aggravated                                  |        |          |          |        |        |
| only first 3 months .....                   | 10 %   | —        | 10 %     | 40 %   | 10 %   |
| 3-9th month .....                           | 2 %    | —        | —        | —      | —      |
| 5-9th „ .....                               | 2 %    | —        | —        | —      | —      |
| No complaints at all during pregnancy ..... | 36 %   | 10 %     | 10 %     | 30 %   | 20 %   |
| Aggravated after .....                      | 90 %   | —        | —        | —      | 10 %   |
| No complaints after .....                   | 10 %   | —        | —        | —      | —      |
| Only complaints during pregnancy .....      | 4 %    | —        | —        | 30 %   | 10 %   |
| Only complaints after .....                 | 6 %    | —        | —        | —      | —      |
| Complaints since pregnancy ...              | 30 %   | —        | —        | —      | 40 %   |

TABLE 6.  
*Skin tests and pregnancy.*  
Studied 25 allergic patients.

|                     | before pregnancy |    |    | during pregnancy |    |    | after pregnancy |    |    |
|---------------------|------------------|----|----|------------------|----|----|-----------------|----|----|
|                     | ++               | +  | —  | ++               | +  | —  | ++              | +  | —  |
| Tuberculin .....    | 10               | 15 | 5  | 2                | 18 | 5  | 16              | 4  | 5  |
| Pollen .....        | 4                | 4  | 17 | 2                | 2  | 21 | 4               | 5  | 16 |
| Housedust .....     | 22               | 2  | 1  | 2                | 22 | 1  | 23              | 1  | 1  |
| Egg-milk .....      | 10               | 7  | 8  | 4                | 12 | 9  | 15              | 4  | 6  |
| Tea-coffee .....    | 5                | 8  | 12 | 2                | 12 | 11 | 6               | 9  | 10 |
| Meat .....          | 8                | 5  | 12 | 6                | 7  | 12 | 9               | 6  | 10 |
| Spinachchicory .... | 15               | 5  | 5  | 10               | 10 | 5  | 14              | 7  | 4  |
| Histamin .....      | 16               | 2  | 7  | 20               | 3  | 2  | 10              | 13 | 3  |

TABLE 7.

*Eosinophilia.*

Studied 25 patients (all examinations are done repeatedly to try to average on normal changes).

| 0-4              | 4-8 | 8 and higher | 0-4              | 4-8 | 8 and higher | 0-4             | 4-8 | 8 and higher |
|------------------|-----|--------------|------------------|-----|--------------|-----------------|-----|--------------|
| 4                | 16  | 5            | 5                | 17  | 6            | 2               | 17  | 6            |
| Before pregnancy |     |              | During pregnancy |     |              | After pregnancy |     |              |

TABLE 8.

*Thorn adrenalin test.*

25 asthmatic patients.

|   |    |    |    |
|---|----|----|----|
| + | 17 | 15 | 9  |
| — | 8  | 10 | 16 |

(In 8 hours at least half of the amount eosinophils must be reached).

TABLE 9.

*17 ketosteroid excretions in 24 hours urine.*

20 asthmatic patients.

|                                 |    |
|---------------------------------|----|
| Constant .....                  | 2  |
| Lowered during pregnancy .....  | 1  |
| Elevated during pregnancy ..... | 3  |
| Lowered after pregnancy .....   | 10 |
| Elevated after pregnancy .....  | 4  |

reactions during pregnancy by hypersensitiveness to food (the diet having been changed as a result of the altered situation). Bray reports having observed a case of asthma, which only appeared during the successive pregnancies. He cites Williamson who claims having observed how the same mother showed no urticaria and food allergy when she was expecting a son, while these conditions did occur when she was expecting a daughter, or vice versa. Klaus Jensen considers induced abortion to be indicated in severe cases of asthma, if a previous pregnancy is known to have resulted in an aggravation, which persisted after parturition. All authors stress the fact that treatment of existing

cases of hypersensitiveness with desensitization etc. should be continued in the normal way.

I should now like to report some personal findings. Although we tried to work as much as possible under identical conditions in a single patient, this is never quite possible in out-patients. For it is known how the site selected for the skin test may be considerably different when compared with another site and how the skin test may be influenced by menstruation, fever, anaesthesia, a period of close contact with or avoidance of the allergen. How often do we not see an injection of pollen result in violent reactions when the patient has a touch of influenza or has caught a cold, while the same dose previously never gave rise to reactions? Therefore it is never entirely possible to avoid all sources of error.

Some results are given from observations in allergic patients (especially asthmatic patients: Tables 5, 6, 7, 8, and 9). As the material was not large enough, the results are certainly not statistically significant. They indicate the necessity of more research, in conjunction with gynaecologists, as it seems very probable that the allergic constitution and reactions are altered under the influence of the sexual hormones.

#### VI. *Therapeutic consequences.*

*Treatment during and after pregnancy.*

- a) The normal development of the foetus should not be disturbed. The mother's fear that any injection might be harmful should be taken into account.
- b) Lactation and the growth of the child may not be harmed.

- I. The normal desensitization treatment is continued as usual. Care should be taken to guard against focal and general reactions, which means that the dosage should only be increased slowly.
- II. *Diet.* A substantial elimination diet is out of the question. A complete prohibition of e.g. any sort of milk (cow, sheep, goat) as a source of calcium is not advisable, even though calcium is added to the diet. Vitamin deficiencies should be counteracted completely. There even is a considerable need for vitamin C. When prohibiting any food the decision should be made whether it may be omitted or whether it should be replaced.

### III. Surroundings during labour.

Guard against new allergens of the bedroom (flowers, stuffings of the bed, dust, chocolate; the patient should slowly become accustomed to eating abundant quantities of eggs and milk).

### IV. Medical treatment.

Eliphyllin adrenalin in low dose. Antihistaminics only when absolutely necessary.

### V. ACTH and cortisone.

The question arises as to whether moderate treatment with decreasing doses of ACTH will not be able to counteract the rapid decrease in adrenal function in those cases in which severe attacks of dyspnoea occur during the first days after labour.

Some cases are reported in greater detail.

- A. A 30-year-old patient. History: positive family history for allergic diseases, the patient herself having had ringworm and vasomotor rhinitis; she came to see me on September 9th and told me that since 1950 *after* the delivery of her first child she had been subject to attacks of dyspnoea (no free interval since then), which are practically limited to 1 week prior to menstruation, and characterized by a slow onset and subsidence.

During her second pregnancy the disturbances were about for the entire period of 9 months, but recurred immediately in a violent form when she was in the lying-in room, until they gradually diminished, appearing again periodically during menstruation. From the fact that she had no disturbances whatever when she saw me she was pregnant again, which could indeed be verified. Blood pressure was 150/100, eosinophilia 9 %. Skin tests for house dust and spinach were markedly positive and those for other inhalation, food, bacterial and hormonal allergens were positive. Thorn's adrenaline test was positive. Three months later the eosinophilia was 8 %.

A satisfactory result was obtained with a treatment directed against house dust and an existing bronchitis and placing of the patient on a diet.

- B. The disturbances do not always appear during the first pregnancy; they frequently first occurred after a 2nd, 3rd or even later pregnancy, although the patient may previously have been affected with allergic manifestations such as ringworm, urticaria or vasomotor rhinitis.

A 40-year-old patient was hospitalized for a chronic asthma with violent exacerbations. The family history and personal history showed that allergic diseases had occurred. When the 2nd child had been born, dyspnoea had appeared; the intervening periods were not free and the condition showed a particular aggravation in the winter. During the period of observation the eosinophilia varied from 3-10 %, while E.S.R. was 1-2 and the blood pressure 110/70. Skin tests: markedly positive for house dust. Intravenous sulphopyretotherapy resulted in the disappearance of the disturbances, whereas a change in bedroom and treatment with exact of house dust and autovaccine failed to alter the condition.

- C. As a result of treatment with autovaccine, extract of house dust and breathing exercises a 34-year-old patient with a long-standing bronchial asthma had practically been without complaints for years. A few days before the birth of her third child the disturbances increased considerably, whereupon they gradually subsided, but still continued to be more violent than before for several months.
- D. A 37-year-old patient had previously been subject to hay fever; ever since her first child had been born she had been affected with a violently itching, disfiguring eczema on the hands, face, axillae and groins, which persisted for 13 years and only disappeared during subsequent periods of pregnancy. A diet based on the results of the skin tests, desensitization treatment with house dust and kapok and treatment with a staphylococcus vaccine afforded relief. Nevertheless the diet and mode of life during pregnancy had been no different. Accordingly the hormonal factor must have been the determining cause.
- E. A 34-year-old patient had been affected with asthma and vasomotor rhinitis ever since she had been 12 years of age. Family history: +. An initial examination revealed an eosinophilia of 14 % and a blood pressure of 120/80. Skin tests were ++ for house dust, + for fungi, pulses, spinach and Brussels sprouts. The disturbances had only disappeared completely during a pregnancy. A violent mental conflict had resulted from a baldness which had been present for the past 10 years. Initially the disturbances showed a very marked increase during her second pregnancy, so that vigorous medical treatment was required. The disturbances diminished after the 5th month and disappeared completely after the 7th month of

pregnancy. The night after labour the first attack of dyspnoea occurred again. From that time on the disturbances persisted. The next violent attack occurred when she saw a child nearly run over. The third violent reaction took the form of an anaphylactic shock when (she had been fasting since 8 o'clock on the previous evening during a Thorn test (8.30 0.3 ml. of adrenaline; 13 hrs. a glass of water for headache)), at 15 p.m., she had an attack of dyspnoea, an imperceptible pulse, asthma and a violent generalized urticaria. She was revived with cardiotonics, antihistaminics and injections of adrenaline. This occurred within a few weeks after labour (lactation had already ceased).

- F. Only one case was observed, in which neither the family history nor the history of the patient herself revealed any evidence of allergic reactions. Attacks of asthma, which mainly occurred at night, appeared immediately after the birth of her first child (which initially proceeded normally; afterwards her 2 eldest children died of a cause which could not be diagnosed, they had been observed in a children's hospital for months on end). At an initial examination for allergy the removal of nasal polyps was recommended. This was not done owing to wartime conditions. When I saw her some years later, I found a chronic bronchitis and a hypersensitiveness to house dust, pulses, fish, salad and grapes. Treatment with house dust, autovaccine, an elimination diet and other general measures failed to produce a sufficient improvement. A combined treatment with ACTH and chloramphenicol, with maintenance doses of cortisone (alternated with intravenous injections of ACTH) was surprisingly successful.

Thorn's test (adrenaline): +.

Total 17-ketosteroids in 24 hours' urine: 5.4.

Eosinophilia: 4-5 %.

- G. Since she had had whooping cough, a 23-year-old patient had been subject to periodic attacks of dyspnoea, especially in the spring and autumn, since she had reached the age of 3. In addition she was affected with vasomotor rhinitis and eczema. The initial examination showed the eosinophilia to be 3 %. Blood pressure 110/80. Skin tests positive for house dust, autumn pollen and rye. No improvement on marrying; during pregnancy the disturbances showed an initial increase and later were practically absent. The disturbances showed an initial increase and later were practically absent.

TABLE 10.  
*Urticaria.*  
Studied 25 cases.

|                                                         |    |
|---------------------------------------------------------|----|
| Disturbances only during the first months of pregnancy. |    |
| Cases with a positive history of allergy .....          | 5  |
| " " " negative " " " .....                              | 20 |

The disturbances did not recur after labour; on the contrary, her state of health continued to be better than ever before. Half a year later the follow up was even discontinued at her request, as she felt so well.

- H. A symptom which is frequently observed, also in women without a history of allergy, consists in a disagreeable urticaria during the first months of pregnancy, which frequently shows a satisfactory response to injections of calcium given by the family practitioner (table 10).

A 31-year-old patient (the family history showed that the mother was affected with urticaria, the patient herself having had intermittent attacks of urticaria several years previously) had been subject to daily attacks of violent itching for the past 2 months (she had been pregnant for almost 3 months), with urticarious wheals covering the entire body and Quincke's oedema of the eyelids. Skin tests were markedly positive for house dust (+++), slightly less for tea (++) and + for numerous vegetables.

Thorn's adrenaline test and total 17-ketosteroids in 24 hours' urine were normal. Treatment with calcium had failed. Treatment with colivaccine and a light diet kept away the disturbances until it could be assumed that they would not appear again.

How are we to explain the effect of pregnancy on allergic diseases? The aggravation may be due to a hypersensitiveness to foreign proteins or hormones; a subsidence of the disturbances might be attributable to hormonal influences.

In the light of our knowledge regarding the favourable effect of ACTH and cortisone one is inclined to believe that the subsidence of the disturbances is due to increased activity of the adrenals, occurring during pregnancy. Obstetrical studies have not supplied any conclusive evidence, however. After a detailed study of the literature Mastboom arrives at the following conclusion: in addition to findings indicative

of a highly unstable equilibrium of numerous functions of the adrenal cortex during pregnancy, clinical investigations furnish evidence suggesting an increased activity of both desoxycorticosteroids and oxycorticosteroids. From his review of the literature we quote: Rasmussen found a hypertrophy of the pituitary (mainly due to an enlargement of the anterior lobe of the pituitary); Kehrer assumes a hyperfunction of the adrenal cortex to be probable during pregnancy; Ferguson observed no difference between Thorn's adrenaline test in pregnant and normal women; Davis and Hulit found a diminished eosinophilic leukocyte count during pregnancy, which was even lower immediately post partum, but this was not observed by Ferguson. Venning, Heard, Parvianen and Talbot, et al. found a progressively increasing elimination of corticosteroids (while it was doubtful which portion was provided by the placenta); Dingemanse and Tain observed an increase in the elimination of 17-ketosteroids, Collard and Heusghem saw no difference, Nuyens found an increase. During the first days of the puerperium the adrenaline test is negative in a far greater number of cases (Ferguson), while the elimination of 17-ketosteroids apparently also shows a decrease (Weher, Nuyens). This may be due to an inhibition of the anterior lobe of the pituitary, resulting from an increased production of steroids with a corticosteroid structure during labour (Sayers, Selye, Sarason). Accurate curves of the eosinophil counts and total 17-ketosteroids in the 24 hours' urine, recorded each day, and repeated investigations at regular intervals with skin tests and Thorn's tests for adrenaline and ACTH may possibly supply a more definite answer to this question. So far the extent to which the adrenals may have an effect on allergic diseases during pregnancy cannot be definitely determined. This will only be possible by a close co-operation with the obstetrician, as our patients are frequently inaccessible to us during these periods.

#### CONCLUSIONS

1. During the first months of pregnancy an aggravation of the allergic reactions or a fresh outbreak (urticaria) is frequently observed.
2. The disturbances frequently diminish slightly after the third and considerably after the fifth month.
3. In some cases the disturbances first appear during the 3rd-5th month, disappearing again after pregnancy.

4. In some cases the symptoms first occur after labour; they show an aggravation or become acute again in many others, or they disappear completely in certain other cases.

5. The intensity of the skin tests decreases after the first months.

6. The eosinophil count does not change during pregnancy, but frequently shows a transient increase after pregnancy.

7. The results of adrenal function tests (Thorn's adrenaline test and determination of the elimination of total 17-ketosteroids in 24 hours' urine) vary during pregnancy and show lowered values after labour. The appearance of allergic reactions post partum might be explained by the considerable decrease in adrenal function resulting from the disappearance of the changes brought about by pregnancy.

8. The therapeutic consequences with regard to the dietary management, flowers, nursing and treatment with cortisone to counteract the decrease are discussed.

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## DISCUSSION

Dr. *Farrerons* (Barcelone):

Hace ya anos estudie el interesante problema de les releciudes entre el ciclo menstrual y el asme en le muyer y no detemos olvidas que durante el ciclo mentrual hay une intensa variaciu en le conducte del sisteme neurovegeteliso en el sentias de une execerbanion durante los dias que preceden a la menstruacion y todes las causas que actuen sobre este sistema adrener pico deten ser teni des en mente pare observar el curso del asme en le muyer gravida, menarguice, puber o durante su ciclo menstrual.

Dr. *Waldbott* (Detroit):

Several cases with premenstrual asthma in my practice had attacks at no other time than before and at the menses. They showed no other features of allergy such as positive skin reactions, eosinophilia.

Their attacks were extremely severe.

After trying many different glandular products. I felt that giving progesterone or prolution prementrually is very effective in these cases.

N. G. M. *Orie* (*A. A. Israels* and *E. E. M. Geelen*):

BRONCHIECTASIS AND ASTHMA BRONCHIALE

## DISCUSSION

Dr. *Williams* (Cardiff):

I was very interested to hear Dr. Orie's most interesting and stimulating paper. I was interested that 62 % of his asthma cases had no pus in the sputum. In England and Wales we find infective asthma as a very common condition in more than 30 % of all our cases. I thought Dr. Orie would be interested in the findings of Professor I. Gough, Department of Pathology, Cardiff. By the large lung section method of Gough and Wentworth he has found in 4 out of 5 consecutive autopsy cases of status asthmaticus—a small area of bronchiectasis—an area which would probably not be shown upon a bronchogram.

Dr. *Bruce Pearson* (London):

Asked Dr. Orie if he felt that he could express an opinion as to whether there was a causal connection between bronchiectasis and asthma or does the asthma cause the bronchiectasis.

Dr. *Eriksson-Lihr* (Helsinki):

I. Did you take the sedimentation rate in consideration in cases with bronchiectasis, where the eosinophile % was lower and in the asthmatic cases, where eosinophiles were higher?

II. Did you make skin tests in these cases. Did you find as many positive skin tests in the cases with bronchiectasis as in bronchial asthma?

Dr. *G. L. Waldbott* (Detroit):

We reexamined our patients on whom bronchograms were made because we had suspected bronchiectasis. They had either lost what we thought was bronchiectasis or they were not allergic. We therefore felt that bronchiectasis in allergic asthma is very rare.

Dr. William's remark concerning the findings of small bronchiectatic areas at autopsy perhaps can bridge the difference in my opinion on this subject. There are perhaps minor bronchiectatic areas in the lungs of allergic asthmatics which remain permanent.

Prof. *L. Businco* (Roma):

ACTION ANTIALLERGIQUE DE LA VITAMINE F

(published N. T. v. G.)

## DISCUSSION

Dr. *Farrerons* (Barcelone):

Nuestra carnística es muy limitada pero tenemos impresion desfavorable de la acción antialérgica de la vitamina F. Repetimos de todos modos que nuestra carnística es muy limitada y ello no quiere decir que su criterio sea erróneo.

G. L. *Waldbott* (Detroit):

"CONTACT DERMATITIS" NEW KODACHROMES

## DISCUSSION

Prof. *M. Ruiter* (Groningen).

THROMBOPHLEBITIS MIGRANS (PANPHLEBITIS  
GRANULOMATOSA MIGRANS)

Prof. *M. Ruiter*, Groningen: Many investigators assume an allergic pathogenesis in cases of thrombophlebitis migrans. The multiple occurrence and episodic character of this disease, together with the fact that no particular micro-organism can be held responsible for the vascular lesions, have been used by various authors as arguments in support of such a hypothesis. Barker found definite focal infections in a large percentage of the patients. Recovery after excision of the gall-bladder, tonsillectomy etc. has been known. Connor and Harkavy described cases which flared up after the use of fish and citrus fruit, whereas an immediate remission set in when their use was discontinued. I myself have tried to find out in how far the histological substrate in thrombophlebitis migrans can furnish further arguments in support of an allergic pathogenesis. The histological examination made in two patients, one of which showed recent lesions, while the other had longstanding lesions revealed a number of changes which may be observed in allergic vascular reactions.

These consisted in:

- a) Reactions of the small vessels, among others in the fatty tissue showing considerable swelling of the endothelium with perivascular infiltration consisting of mononuclear cells. The same changes were observed in the nutrient vessels of the medium-sized veins.
- b) Peculiar endothelial changes in the smaller and medium-sized veins, in the form of swelling, proliferation and dissociation of

the endothelium layer (the so-called "strang- und bogenförmige Endothelwucherung" of German allergists).

- c) Presence of typical intimal granulomas in the affected medium-sized veins.
- d) Marked eosinophilia of the inflammatory tissue.
- e) The presence in one of the cases of small bloodvessels with fibrinoid necrosis.

No micro-organisms could be demonstrated in the histological sections.

Histological changes observed more or less regularly in allergic inflammatory reactions should be judged with care. In our opinion, however, the simultaneous occurrence of a number of these characteristics, as encountered in the course of this histological examination, strongly suggests an allergic pathogenesis, the more so as the clinical picture, the clinical course etc. in thrombophlebitis migrans furnish additional arguments in favour of this hypothesis.

As to the aetiology, I wish to confine myself to 6 personal cases, in which the diagnosis was also confirmed by histological examination. Four of these patients were found to be affected with active tuberculosis. This incidence cannot very well be considered as a coincidence. As the histological picture of the vascular anomaly does not indicate tuberculosis in a stricter sense, the possibility of an allergic reaction to a tuberculous antigen should be taken into account in some cases. Parallergic or hetero-allergic reactions in these tuberculous patient should, however, also be considered. In non-tuberculous cases various antigens probably play a part (micro-organisms, food-antigens, tobacco allergens etc.).

The histopathological changes in thrombophlebitis migrans are rather characteristic. The proliferative character of the inflammatory reaction of the affected veins was an outstanding feature. This may be expressed by the term panphlebitis granulomatosa migrans. The histopathological substrate was similar in various respects to the one found in thromboangiitis obliterans. Personally I hold the view that there is a relationship between the two syndromes.

(To be published in detail in "Arch. für Dermat. u. Syph.")

#### DISCUSSION

Prof. *Businco* (Rome):

Je veux me complimenter avec M. le Prof. Ruiter pour la belle démonstration qu'il nous a donné sur ce cas de thromboangiitis migrans,

C'est bien peu souvent qu'on peut admirer des sections histologiques si claires et si probatives.

Nous avons étudié à Rome, avec M. le Prof. Lucherini, un cas de tromboangiitis migrans avec des referts histologiques tant à faits égaux. Dans les études des lésions initiales, nous avons trouvé les altérations typiques de l'inflammation allergique. Nous sommes de l'avis que la pathogénèse de la maladie c'est certainement allergique.

*J. F. Farrerons* (Barcelona) :

ROLE OF THE FOOD ALLERGY IN THE ADULT'S  
BRONCHIAL ASTHMA

(published N. T. v. G.)

*F. W. Wittich* (Minneapolis) :

RECENT TRENDS IN ALLERGY THERAPY

*W. J. Quarles van Ufford*,  
Utrecht.

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