

# CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

## *Case Reports and Observations*

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Urticaria is a lesion familiar to almost everyone and has been described in the medical literature since the time of Hippocrates. Yet the cause of chronic hives is frequently baffling and the treatment often unsatisfactory. No therapy may be necessary for acute hives, although abstaining from food for twenty-four hours, purgation and adrenalin hypodermically will probably result in more prompt relief. Chronic urticaria presents an entirely different problem, as is illustrated in the following case reports. No attempt is made to distinguish between urticaria and angioneurotic edema except in diagnosis, because the lesion is essentially the same in either case. In fact, both frequently occur in the same individual and the causes and treatment are similar.

*Case 1:* The patient was a housewife twenty-six years of age, who complained of recurring attacks of localized edema for the past three years, involving the feet, hands, fingers, arms, lips, and eyelids. The attacks occurred ten to fourteen days prior to the menstrual period and lasted about five days. The areas were painful and at times blood was vomited during the attacks. She felt sure that taking aspirin would precipitate an attack. The personal history otherwise was negative for allergic disease. Her father had similar attacks of edema, which he attributed to the use of aspirin.

Physical examination was relatively negative. Routine blood counts and urinalysis were normal. Roentgen examination of the gastro-intestinal tract showed a normal stomach, gallbladder and colon.

Allergy studies revealed sensitivity to feathers, house dust, orris root, brewer's yeast, cow's milk, corn, cherry, plum, and to several other less frequently used fruits and vegetables.

On a program of avoidance of the inhalants and foods to which she reacted, as well as the drug she suspected, she became free from symptoms. A letter two years later stated that she had slight attacks of swelling only when she failed to follow the allergy diet. She was using goat's milk as a substitute for cow's milk. The angioneurotic edema in this case was apparently due chiefly to foods, though a drug (aspirin) would precipitate an attack also.

*Case 2:* The patient, a woman twenty-five years of age, was seen in April, 1938, complaining of headaches and hives. The headaches had been present for some time, but for the preceding six months they had been very severe, lasting three days and recurring about twice a month. She usually had a headache during or after the menstrual period, and a second headache in the intermenstrual period. They were the hemicrania type, and accompanied by no gastro-intestinal upset except for a tendency to constipation during the attacks. The hives, which were usually on the face, neck, and arms, had been present almost daily for several years. As a rule, the lesions were few and lasted only a few hours, although they were quite itchy and annoying. She also exhibited a tendency at all seasons for easy sneezing, nasal obstruction and postnasal mucoid discharge. Her mother and sister had similar headaches, while her father and a maternal aunt suffered from asthma.

## C. R. K. JOHNSTON

Physical examination was entirely negative. The routine urinalysis and blood counts were negative except for a mild anemia (hemoglobin 69 per cent). The eosinophil count was 2 per cent.

Allergy investigation revealed sensitivity to numerous inhalants, including feathers, dust, orris root, tobacco, silk, and several animal danders. The food reactions were quite marked to wheat, white potato, pineapple, brewer's yeast, cherry, strawberry, and Brussels sprouts, and less marked reactions to egg, milk, and many others.

On a regime of avoidance of the significant inhalants and foods, she made marked progress. Three months after beginning the regime, she reported that she had had no hives, and the headaches were much improved. Those headaches she had had could be attributed to a break in her diet.

Twenty-two months after the institution of the allergy program, she was still free of hives. She had had only one attack of giant hives, this following the ingestion of three empirin compound tablets. The headaches also were completely gone except on a few occasions when she broke her diet. She had found that eating white potatoes or wheat would result in headaches, as well as hives. Both the migraine and urticaria in this case could be attributed to foods. A drug (empirin compound) had also precipitated an attack of hives on one occasion.

*Case 3:* The patient, a woman twenty-six years of age, complained of swelling of the lips, the right side of the forehead and the right forearm. The swelling had been present almost three years and occurred in close relation to the menstrual period, either just before, after, or during the period. Headache and nausea always accompanied the attacks. About one year prior to her visit, following an attack of pain in the right side, she had the appendix and right ovary removed. From the time of the operation to the present attack she had had only one subsequent attack of angioneurotic edema. Various elimination diets in the past had failed to help.

With the exception of the areas of angioneurotic edema, physical examination was entirely negative, as were the routine blood counts and urinalysis.

Because of the obvious relationship of her attacks to the menstrual periods, allergy tests were omitted and glandular therapy given a trial. She was advised to have 1 cc. of antuitrin S (100 units per cc.) daily for five to seven days, beginning about ten days before the period was expected. This was carried out for two consecutive periods, during which time no swelling occurred. The therapy was stopped and she remained free from attacks for the next three months as well. The edema then recurred, involving the same three sites as before. She was advised a similar program, this time using A. P. L., (Ayerst, McKenna, and Harrison) in doses of 1/5 cc. (500 units per cc.). For approximately five months this program was continued. About five doses of the A. P. L. preceding each period were taken, and she remained free of edema. This freedom continued for five months after taking the last dose of A. P. L. when once more the edema recurred in the same areas. She was again advised to resume the same type of therapy and has not returned, although over a year has elapsed since the last visit. This patient's angioneurotic edema was controlled by treating only the endocrine factor.

*Case 4:* The patient, a man aged forty-two, came to the Clinic because of hives and headaches. The hives had begun some three and one-half years previously, at which time he was in apparently good health. He was an auditor and was working hard and under considerable nervous tension. Attacks had occurred almost every day since the onset, the only free period being for one or two days while on a brief vacation. The hives were generalized at first; later

## CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

they recurred more often on the back and upper chest. No angioneurotic edema was present. The hives were worse during the day, while at work, and bromides would give some relief.

He took a proprietary preparation, containing antipyrine, potassium bromide and sodium salicylate, one or more times per week for headache but used no other drugs. An interesting observation was that he had seen thirteen doctors for the above complaint before consulting the Clinic. He had found that eating eggs would cause hives but no other foods were suspected.

Since childhood he had had severe generalized headaches, recurring on the average of once a week, and lasting about twenty-four hours. Until some fifteen years ago they had been accompanied by nausea and vomiting. Since then nausea occurred but rarely. Substituting kapok pillows for feather pillows had resulted in some improvement and wearing glasses also helped, but the headaches continued.

The personal history was otherwise negative for allergy. His mother had "sick headaches," and her mother and brother had asthma. A paternal aunt had hay fever.

Physical examination revealed a well developed and nourished, apparently healthy individual. Several urticarial wheals were present on his back and his skin exhibited a mild dermatographia. The physical examination otherwise was not significant.

Dental examination revealed a retained root, one devitalized tooth, and two molars which showed questionable apical involvement. Routine blood counts and urinalysis were normal. Blood eosinophilia was not present.

Allergy studies by the scratch method were all negative. Intradermal tests showed immediate reactions to many inhalants, including kapok 3+, house dust, feathers, orris root, tobacco, silk, cat and dog dander 2+, and 1+ readings for pyrethrum, mattress dust, yeast and several molds. Delayed reactions were 2+ to oidiomycin and 4+ to trichophylin. No significant reactions were obtained to bacteria. Many positive food reactions (chiefly 1+) were found, including corn, oat, pork, duck, goose, turkey, coffee, tea, chocolate, the berry group, onion, asparagus, mushroom, nuts, canteloupe, cucumber, watermelon, and olives.

A very careful program of treatment was outlined, including avoidance as far as possible of all inhalant and food allergens. He was instructed to avoid rigidly the use of the proprietary he had been taking and all other drugs. Hypo-sensitization therapy was begun for the inhalant allergens, including dust, feathers, orris root, kapok, tobacco smoke and ashes and the significant molds, all in a 1:10,000 concentration. He was strongly advised to obtain extra rest, have the dental foci removed, and was temporarily given a sedative of bromides and belladonna.

One month later the patient stated that his headaches had ceased and that the hives were much improved. Further extract was supplied and the above program continued.

Five months after beginning this treatment, the patient returned and reported that he had only an occasional hive and seven to ten days would pass without any at all. The headaches were almost entirely absent, although an occasional, mild ache still occurred. He reported one severe flare-up in hives after a dose of concentrated extract (1:10) and he had found that inhalation of tobacco smoke or orris root would precipitate an attack of hives in about half an hour.

In this case the urticaria may have been due to one or several factors. Food and inhalant allergy seem definitely incriminated, but a proprietary, fatigue, and focal infection may also play a definite role.

### DISCUSSION

In cases of urticaria and angioneurotic edema, skin tests are admittedly of less value than in other allergic diseases. Investigation of patients complaining of either of these lesions must be very thorough, and all possible factors should be treated if one is to achieve satisfactory results. In a small number of cases, the history may strongly incriminate a significant factor, such as the endocrine factor in Case Three, or some drug frequently taken by the patient. Skin tests may be postponed in such a case until a trial of removal of the suspected food or drug or control of the glandular factor has been attempted and if successful, allergy tests may not be necessary. Seldom, however, is the problem solved so simply.

When the history indicates the coexistence of one or more allergic manifestations (Cases 2 and 4), or a family history of allergy (Case 1), the greater is the likelihood that the case under investigation will prove to be on an allergic basis. Such allergy usually is dependent on food, drug, or bacterial sensitivity, but occasionally it may be due to inhalants or physical agents. The foods commonly incriminated include milk, eggs, wheat, chocolate, shellfish, and many others. Drug allergy is frequent and includes many widely used drugs, such as aspirin and other salicylates, phenolphthalein, quinine, ipecac, barbiturates, opium derivatives, iodides, etc. Focal infection is undoubtedly a common cause of chronic hives and it may be explained on a basis of bacterial toxins or bacterial sensitivity. Search should always be made for foci in teeth, tonsils, sinuses, gallbladder, appendix, prostate, etc. In some cases where no focus can be found, we have had considerable success with bacterial vaccines made from stool cultures.

When the personal and family history are entirely negative for allergic disease, many allergists believe that drugs or foci of infection are the most likely causes. The psychogenic factor is also important. It may at times be primary, and frequently is a contributing factor of significance. I feel that thorough testing should be carried out in these cases, however, as food or other allergy also may be present and its removal will lighten the "allergic overload." It is not infrequently noted that certain foods will cause an increase in symptoms, although the removal of these foods from the diet may not result in disappearance of all hives. The endocrine factor is probably not of great significance as a primary cause although it may contribute secondarily in many cases in the form of lowered metabolic rate, for example, or in women nearing the menopause.

## CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

In conclusion, I should like to emphasize that chronic urticaria or angioneurotic edema may have many causative factors, either primary or secondary. A few illustrative case reports have been given, although needless to say, the conclusions are by no means based on these alone.

It seems worthy of emphasis that when a personal or family history of other allergy exists, the cause of hives or angioneurotic edema is more likely an allergic one. In the absence of any allergic history, drug allergy or focal infection are very frequent offenders. The psychogenic factor is an important one, although I believe every attempt should be made to rule out other causes before one admits this to be the primary factor.