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Update

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Chronic urticaria

by John Oppenheimer, M. D., and Charles Kirkpatrick, M. D.

The Florida patient not only was chronically ill; he was chronically angry and upset with the health care system.

For two years he had endured daily outbreaks of urticaria. His life was severely disrupted by his condition, which was poorly responsive to therapy. He had consulted several medical experts, none of whom could identify the underlying cause. Finally, physicians at the Scripps Clinic referred him to the National Jewish Center for Immunology and Respiratory Medicine.

Admitted as an inpatient, the man was placed on a fast, subsisting on a non-allergenic protein drink for five days. Within 48 hours, the hives were gone. Further tests pointed to a probable precipitating factor, and subsequent modifications in the patient's diet confirmed what we had suspected: the urticaria had resulted from an allergy to wheat.

More than a nuisance

As the above story illustrates, chronic urticaria can be a vexatious problem for both patient and physician.

Urticaria is "a vascular reaction,

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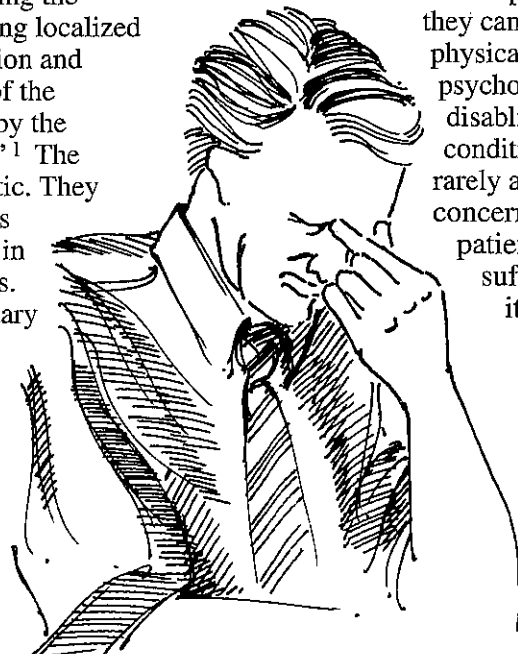
usually transient, involving the upper dermis, representing localized edema caused by dilatation and increased permeability of the capillaries, and marked by the development of wheals."¹ The lesions are usually pruritic. They vary in size from papules measuring only 1-2 mm in diameter to large plaques. Excoriations and secondary infections may be present. By definition, individual urticarial lesions last no longer than a day, and usually resolve in two to four hours.²

Urticaria can be accompanied by

angioedema, a reaction in which the edematous process extends through the dermis and into the subcutaneous or submucosal tissue. Angioedema usually affects the face and extremities, but may involve the throat and cause obstruction of the airway.

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Pathogenesis

Urticaria can be mediated by both immunologic and non-immunologic factors. The underlying mechanisms are not well understood, but the final common pathway is believed to involve release of mediators by activated mast cells and basophilic leukocytes. These mediators increase vascular permeability, and plasma leaks into the dermis, resulting in urticarial wheals.²

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Immunologic reactions which do not involve IgE include hereditary angioedema and acquired angioedema, which are complement-mediated, and type III hypersensitivity reactions, caused by circulating immune complexes. These disorders rarely, if ever, present as typical urticaria.

Many chemicals may trigger urticaria through non-immunologic mechanisms. They include aspirin, thiamine, codeine and morphine, among others.³ Physical stimuli (heat, cold, vibration, etc.) can release histamine and other mediators through immunologic, non-immunologic or a combination of means.⁴

Diagnostic evaluation

In many cases of acute urticaria, the source is obvious or the physician and patient stop looking for it upon remission. With chronic hives, however, identifying the triggering factor can take on a special urgency and is often necessary for long-term control of the disorder. Unfortunately, uncovering the cause of chronic urticaria is frequently difficult because, as in the case cited above, the triggering agent is ubiquitous or not regarded as a medication or food, and contact with it is deeply ingrained in the patient's lifestyle. Urticaria also can result from a combination of factors, e.g., eating a particular food and then exercising (a condition known as exercise-induced urticaria); so the process of diagnostic evaluation can be complex.

The diagnosis of urticaria is one of exclusion. It is essential to rule out the presence of serious illnesses of which recurring hives can be a symptom. Examples are hepatitis, hyperthyroidism, lymphomas, lupus,

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The history is the most important part of the initial evaluation. The patient should be asked whether the onset of urticaria seems to be associated with specific substances or events. Some of the most common causes of urticaria are listed in Table 1. If an interview fails to generate satisfactory insight, it can be helpful to have the patient keep a diary recording outbreaks,

foods eaten, drugs taken, environmental factors and activities.

Occupation can play a part in urticaria and should be considered in establishing the diagnosis. For example, carpenters and butchers often experience pressure urticaria and angioedema on their hands and the soles of their feet because of frequent or constant stress on those areas. Likewise, urticaria patients with sedentary jobs often get hives on their buttocks from the pressure of sitting. These "delayed pressure" urticarias may be manifestations of food allergy.

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Inpatient admission for diagnostic evaluation can be highly beneficial, especially when food is suspected as the cause of urticaria. In such cases, hospitalization assures control and compliance with the diet. When elimination diets are used on an outpatient basis, even the most conscientious individuals often fail to adhere strictly to the rules. (An example from our own experience was a patient who had taken Alka Seltzer nightly for so long that he was barely conscious of the habit.) It's also helpful to be able to offer the encouragement and support a patient needs to stick with a fasting regimen, as well as to observe urticaria lesions when they occur.

In the case of the man from Florida referred to National Jewish, once the fast established that food allergy was responsible for his urticaria, a reaction to wheat on a skin test indicated the strong possibility that eliminating this antigen from the patient's diet would improve the problem.

Penicillin, aspirin and sulfa drugs are the medications most commonly associated with urticaria, but this reaction can happen with almost any

drug. Most in vitro drug tests are not reliable for determining allergic reactions. That is why, as in assessing food allergies, an empirical approach is best.

At National Jewish, we find that five to seven days in the hospital is usually sufficient to uncover the etiology of chronic urticaria if a cause can be found. As a specialty referral center, we have one of the nation's outstanding clinical immunology labs, excellent skin-testing facilities and an array of other state-of-the-art diagnostic resources, allowing us to pinpoint the etiology of chronic urticaria in a number of patients who otherwise would not be properly diagnosed.

Treatment

Eliminating the etiologic agent is the best way to treat chronic urticaria. Avoiding exposure to

ubiquitous substances such as wheat or food additives can be difficult, but is usually well worth the trouble. While patients are at National Jewish, and after discharge, nutritionists and other staff may work with them and with referring physicians to help establish new diets, environmental controls and other therapeutic regimens.

Even when the causes of chronic urticaria cannot be found, drug therapy enables most patients to live normal lives. Medications are prescribed to provide relief by preventing or minimizing symptoms. It is important to emphasize that patients should take the prescribed dose and not use the medication on an "as-needed" basis.⁶

In most cases, antihistamines diminish pruritus significantly, and although they do not always reduce the number of urticarial lesions or

the frequency of eruptions, no other intervention is required. Patients can sometimes tolerate the side effects of one antihistamine better than those of another, even with comparable doses.⁶ Often a combination of H-1 and H-2 antihistamines gives better results. Promising clinical studies in this area are being conducted by National Jewish physician Alan L. Schocket.

At National Jewish, we try to avoid long-term therapy with corticosteroids, although we appreciate their value for short-term relief. If antihistamines fail, other drugs such as beta adrenergic agonists, antiserotonin drugs, hydroxychloroquin, etc., deserve evaluation.

The medical staff at National Jewish includes a group of physicians with a specific interest in urticaria. They encounter many more cases than are seen at most community or even university hospitals, and therefore have special expertise in diagnosis and treatment. More importantly, they are able to conduct research to improve the understanding and management of this fascinating condition.

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Table 1
Some common causes of urticaria²

Drugs and chemicals

- Salicylates
- Indomethacin and other nonsteroidal anti-inflammatory drugs
- Opiates
- Radiocontrast material
- Penicillin (medication, milk, bleu cheese)
- Sulfonamides
- Sodium benzoate
- Cosmetics
- Douches
- Ear or eye drops
- Insulin
- Menthol (cigarettes, toothpaste, iced tea, hand cream, lozenges, candy)
- Tartrazine (vitamins, birth control pills, antibiotics, TDC yellow #5)
- Food additives

Foods

- Nuts
- Berries
- Fish
- Seafood
- Bananas
- Grapes
- Tomatoes
- Eggs
- Cheese

Contactants

- Wool
- Silk
- Substances in the occupational environment
- Potatoes

Cosmetics

- Dyes
- Hair spray
- Nail polish
- Mouthwash
- Toothpaste
- Perfumes
- Hand cream
- Soap
- Insect repellent

Physical stimuli

- Dermatographism
- Light
- Pressure
- Heat
- Cold
- Water
- Vibration

Inhalants

- Animal danders
- Pollen

Infections

- Bacterial
- Dental abscess
- Sinusitis
- Otitis
- Cholecystitis
- Pneumonitis
- Cystitis
- Hepatitis
- Vaginitis

Fungal

- Tinea
- Candida

Other

- Scabies
- Helminth
- Protozoa
- Trichomonas

Systemic diseases

- Rheumatic fever
- Juvenile rheumatoid arthritis
- Leukemia
- Lymphoma
- Collagen vascular disease

Endocrinopathies

- Hyperthyroidism
- Menstruation
- Hormones

Daily CME Conferences

Daily continuing education conferences on pulmonary and immunologic topics are conducted at National Jewish in Heitler Hall. All physicians in the community, as well as those visiting Denver, are welcome to attend. For information about specific topics and times, call (303) 398-1380.

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