INTRODUCTION

Urticaria is a common disorder affecting approximately 15 to 20% of the general population at least once during their lifetime. Although it may occur at any age, it is most frequent in the age group of 20-40 years. Allergenic triggers can be identified in up to 60-80% of acute urticaria cases while this figure is much lower for chronic urticaria. Chronic urticaria has multifactorial etiologies including autoimmune processes, intolerance to food or drugs, infectious diseases etc ***(Greaves, 2003).***

Approximately 50% of chronic urticaria cases remain unexplained and are categorized as chronic spontaneous urticaria while the remaining 50% have an autoimmune basis ***(Guerra et al., 2007).***

Several recent studies have shown that contact allergy can play a role in the etio-pathogenesis of chronic urticaria ***(Guerra et al., 2007).***

Several reports showed that chronic urticaria was subsequently found to be caused by common contact sensitizers like nickel, chromium, cobalt, balsam of Peru and rubber chemicals ***(Piskin et al., 2003).***

Interestingly, such patients with chronic urticaria do not exhibit the physical signs for contact allergy ***(Sharma, 2008).***

Urticaria, at least a sub group of it, can have a delayed type reaction component which may be explanatory to many patients. Still there are patients with

chronic urticaria without a detectable underlying etiologic factor and they need further work up to reach diagnosis ***(Kaplan, 2002).***

Because of the heterogeneity of urticaria and its many subtypes, guidelines for diagnosis might start with a routine patient evaluation, which should comprise a thorough history and physical examination, and the ruling out of severe systemic disease by basic laboratory tests ***(Zuberbier et al., 2010).***

Specific provocation and laboratory tests should be carried out on an individually on the basis of the suspected cause ***(Zuberbier et al., 2006).***

Prick test is sometimes done during the etiologic work up of chronic urticaria. Prick test helps in diagnosis of IgE mediated urticaria. However, allegro-logists are often confronted with unclear and inconclusive results, e.g. due to cross-reactivity, or non-IgE mediated allergies ***(Jacob and Steele, 2006).***

Patch test is one of the allergy tests that relies on the principle of a type IV hypersensitivity reaction and late phase of type I hypersensitivity reactions ***(Turjanmaa et al., 2006).***

It is a method used to determine if a specific substance causes allergic inflammation of the skin. In chronic urticaria skin prick tests are recommended for the etiologic work up while patch tests are not ***(Sharma, 2008).***

Previous studies showed that some patients with chronic urticaria without a detectable underlying etiologic factor can have positive skin patch test results ***(Avneet and Pramod, 2014).***

Aim of the Work

The aim of this study is to investigate the possible significance of patch test with common allergens in diagnosis of chronic spontaneous urticaria.

CHAPTER (1): URTICARIA

Definition of Urticaria:

Urticaria is a common dermatologic condition, characterized by erythematous wheals caused by mast cell degranulation and histamine release. Approximately 15% to 25% of the population is affected at some point in their lifetime causing a significant disturbance in quality of life ***(Poonawalla and Kelly, 2009).***

Commonly it referred to as hives, appears as raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis that are very pruritic. It may be acute (< 6 weeks) or chronic (>6 weeks) ***(Frigas and Park, 2009).***

Historical point of view:

Urticaria, commonly called 'hives,' has a long and rich history in documented medicine dating back at least to the 10th century B.C. when it was called 'Feng Yin Zheng' in China ***(Rook, 1974).***

Many cultures have described urticaria in some capacity and the disorder has had many names. In the 4th century B.C., Hippocrates noted the similarities between urticaria, contact with stinging nettles, and insect bites and called the condition 'cnidosis' (nettle rash) ***(Humphreys, 1997).***

'Uredo,' 'essera' (Arabic for elevation), 'urticatio' (derived from the Latin urere; to burn), and 'scarlatina urticaria' have all been used ***(Humphreys, 1997).***

Use of the term 'morbus porcinus', which means pig's disease, resulted from a translational error of the intended term 'morbus pocellaneus,' which referred to the white color of the central wheal ***(Czarnetzki, 1989).***

Epidemiology:

Race

Urticaria is a worldwide disease and may present at any age ***(Schafer & Ring, 1993).***

Sex

Incidence rates for acute urticaria are similar for men and women; chronic urticaria occurs more frequently in women (60%) ***(Peroni et al., 2010).***

Age

Urticaria can occur in any age group, although chronic urticaria is more common in the fourth and fifth decades ***(Peroni et al., 2010).***

Chronic urticaria (CU) refers to continuous or intermittent wheals existing for 6 or more weeks that may be caused by physical stimuli, allergy, systemic illness, drugs, or infection, however, in the majority of cases (80%-90%), no eliciting cause is identified and recently, researches show no evidence of an exogenous allergens the cause of CU which is labeled chronic spontaneous urticarial ***(Zuberbier et al., 2009).***

In recent years, 30% to 50% of patients with CSU have been shown to have an autoimmune cause of histamine release leading to recurrent hives ***(Godse, 2004).***

CSU is twice as common in women as in men. Although persons of any age may experience CSU, it occurs most frequently after adolescence, with the highest incidence in young adults in the adult population ***(Gaig et al., 2004).***

Etio-pathogenesis:

Information regarding history of previous urticaria and duration of rash and itching is useful for categorizing urticaria as acute, episodic (recurrent), or chronic ***(Kanani et al., 2011).***

Classification of Urticaria: *(Kanani et al., 2011)* (Fig. 1)

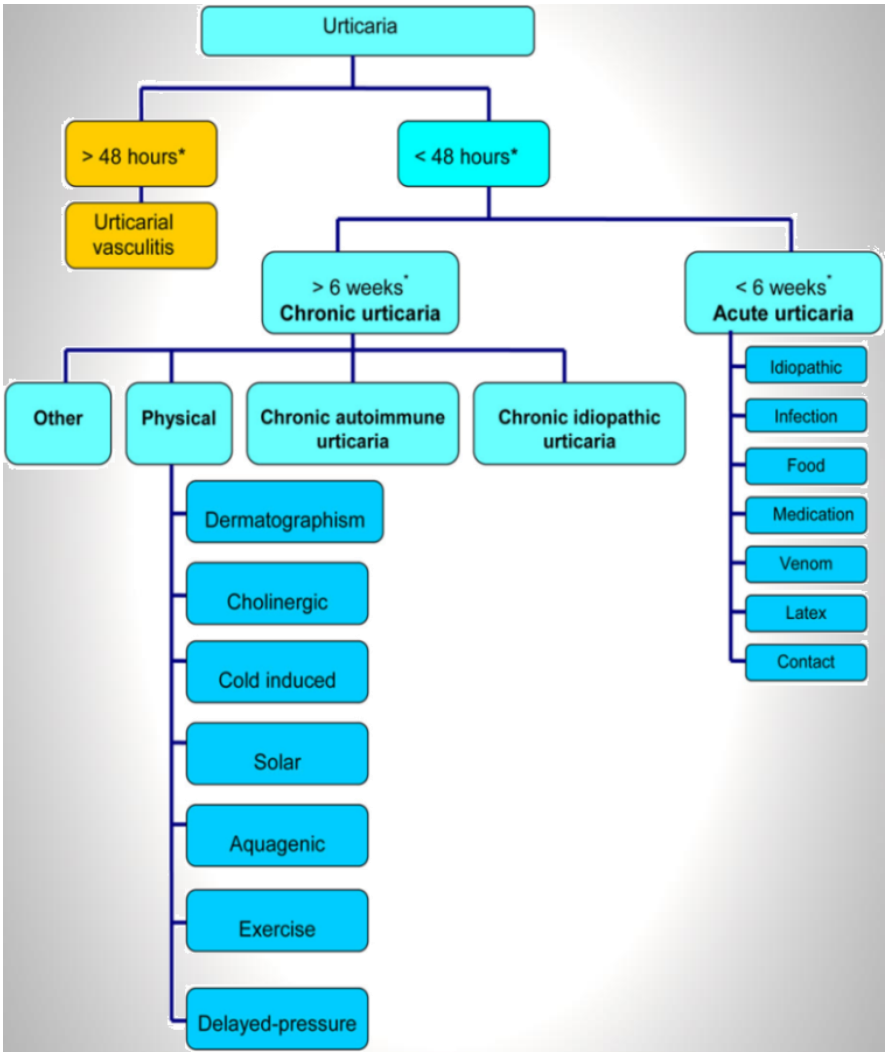

Fig. (1): Classification of urticaria: overview. *The 48-hour cut-off refers to individual lesions, while the 6-week cut-off refers to the condition as a whole.

Aetiologic classification:

1- Immunological:

A-Autoimmune (Autoantibodies against FceR1 or IgE):

Recent data suggest that 35-50% of chronic urticaria cases are related to autoimmunity specially the presence of autoantibodies to the high affinity IgE constant fragment receptor-1(FceR1) located on mast cells ***(Hide et al., 1993).***

This can result in chronic stimulation of these mast cells and release of vasoactive mediators. Autologous serum skin test can separate these patients from the remaining idiopathic cases ***(Hide et al., 1993).***

B-Allergic: **(fig. 2)**

Which is considered (IgE-mediated type I hypersensitivity reactions):

The difference between a normal infectious immune response and a type-1 hypersensitivity response is that in type-1 hypersensitivity the antibody is IgE instead of IgA, IgG, or IgM. During sensitization, the IgE antibodies bind to Fce receptors on the surface of tissue mast cells and blood basophils. Mast cells and basophils coated by IgE antibodies are "sensitized" ***(Kobayashi et al., 2001).***

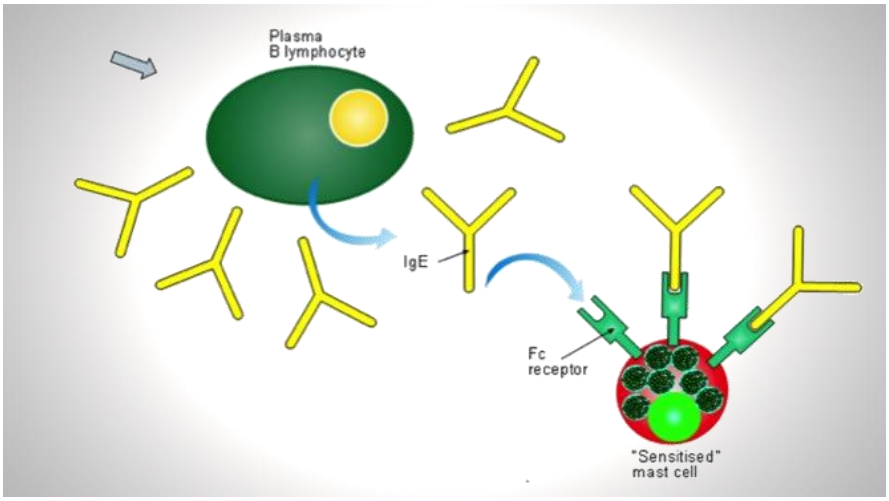

Fig. (2): Primary exposure

Later exposure to the same allergen cross-links the bound IgE on sensitized cells, resulting in degranulation and the secretion of pharmacologically active mediators such as histamine, leukotriene (LTC4 and LTD4), and prostaglandin that act on the surrounding tissues. The principal effects of these products are vasodilation and smooth-muscle contraction ***(Kobayashi et al., 2001). (fig. 3)***

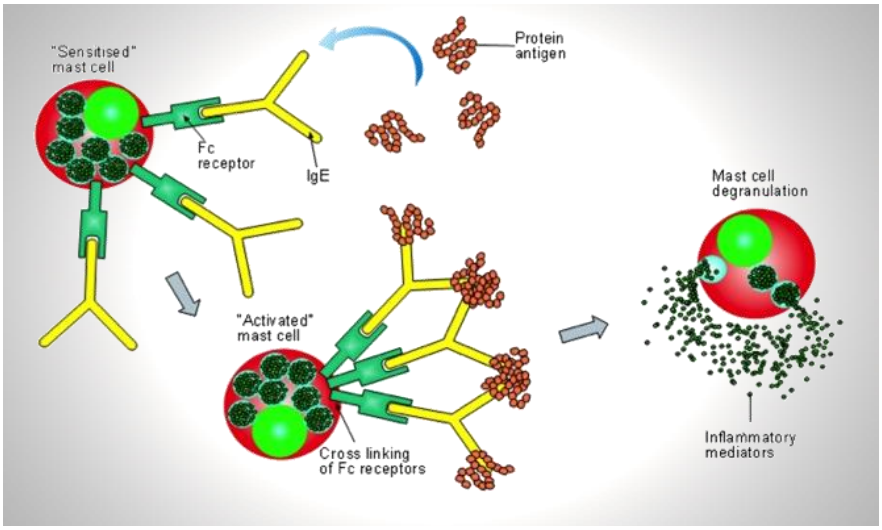

Fig. (3): Re-exposure

Type-1 hypersensitivity can be further classified into an immediate and late-phase reaction. The immediate hypersensitivity reaction occurs minutes after exposure and includes release of vasoactive amines and lipid mediators, whereas the late-phase reaction occurs 2–4 hours after exposure and includes the release of cytokines ***(Kobayashi et al., 2001).***

Common allergens include:

1. **Foods**:

   Tree nuts, fish, eggs, milk, soy, wheat, and banana.

2. **Organic substances:**

   Preservatives, latex, hymenoptera venom., etc.

3. **Chemicals:**

   Nickel, cobalt, paraben, etc.

4. Medications:

Penicillin, cephalosporin, aspirin, NSAIDs (direct histamine releaser), etc

5. Aeroallergens:

Dust mites, pollens, molds and animal dander ***(Kaplan and Greaves, 2009)***.

Cobalt can also found in jewelry, dental implants, artificial joints, jet engines. Most patients are also allergic to nickel, and some are also allergic to chromate.

As regard **nickel,** 10 per cent of women and at least 1 per cent of men are affected by nickel allergy. Nickel is released from metals such as alloys or electroplated items. Found in jewelry, keys, coins, zips and buckles, pacemakers and batteries.

Parabens is preservatives found in cosmetics and topical medical products to inhibit the growth of fungi and prevent slow deterioration. They are commonly used in cosmetics, household products, glue, shoe polish, shampoos and conditioners, sunscreens and medical creams.

Neomycin is an antibiotic commonly used in ear and eye drops and creams to treat infected skin problems. Cross-reacts with other antibiotics.

Aspirin: as a drug, and also present in some food, like: blueberries, cherries, dried currants, curry, dry dates, pickles, licorice root, prunes and raspberries. Moderate amounts of salicylates include almonds, apples (especially

the variety Granny Smith), oranges, peppers (sweet and hot), dates, plum, pineapple and tea.

Latex: present in many Products, "**Medical Products & Household Products":**

Medical products like:

- Urinary catheters,
- Stethoscope tubing
- Endotracheal Tubes, ,
- Tourniquet Condoms – Diaphragms,
- Ambu bags, Band-Aids,
- Ventilator bellows,
- Masks (anesthesia, oxygen), Gloves (unless stated on label or box,
- Adhesive tapes, Blood pressure cuffs,
- Nasal airways,
- Elastic on surgical bonnets or shoe covers,
- Rubber bands,
- Elastic bandages, Toy balls ***(Kumar, 2012).***

House holds produscts:

- Rubberized bed sheets, Swim caps/ some goggle straps, Wheel chairs cushions and tires
- Carpet backing
- Hot water bottles,

- Baby bottles,
- Rubber toys,
- Shower curtains / mats / & other rubber mats
- Balloons,
- Cleaning gloves ***(Kumar, 2012)***

C- Urticarial vasculitis:

Urticarial vasculitis is a relatively rare diagnosis in a patient presenting with urticaria. Urticarial vasculitis is an eruption of erythematous wheals that clinically resemble urticaria but histologically show changes of leukocytoclastic vasculitis ***(Oi et al., 2005).***

Urticarial vasculitis is a type III hypersensitivity reaction in which antigen-antibody complexes are deposited in the vascular lumina. This reaction results in complement activation and chemotaxis of neutrophils. These cells release various proteolytic enzymes, such as collagenase and elastase, resulting in damage to the vascular lumina ***(Kallenberg, 2008).***

Urticarial vasculitis may be divided into normocomplementemic and hypocomplementemic variants. Both subsets can be associated with systemic symptoms (eg, angioedema, arthralgias, abdominal or chest pain, fever, pulmonary disease, renal disease, episcleritis, uveitis, and Raynaud phenomenon). The hypocomplementemic form more often is associated with systemic symptoms and has been linked to connective-tissue disease (ie, systemic lupus erythematosus [SLE]) ***(Venzor et al., 2002).***

2- Infections:

Includes: Viral (e.g. cytomegalovirus, Epstein-Barr, hepatitis), parasitic, fungal, or bacterial (e.g. H pylori). Recent evidence suggests that Helicobacter pylori infections play a role in the pathogenesis of a variety of skin diseases including urticaria The best evidence for such a link is found for two diseases: chronic urticaria and immune thrombocytopenic purpura ***(Hernando-Harder, 2009).***

3- Physical urticaria:

There are different types of physical urticaria. The reason why a rash appears in affected people is not clear. The physical stimulus somehow causes a release of histamine and other chemicals, which causes the rash. The main types of physical urticaria include the following.

a) Dermographism: Means skin writing. People with this condition develop the rash on areas of skin that have been firmly stroked. Firm stroking of the skin produces an initial red line (capillary dilatation), followed by an axon-reflex flare with broadening erythema (arteriolar dilatation) and the formation of a linear wheal (transudation of fluid/edema); these events are collectively termed the triple response of Lewis. Although any part of the skin can be affected, the palms, soles of the feet, genital skin and scalp are less commonly affected. ***(Grimm et al., 2000).***