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Gloves to Balloons

Incidence of Latex Allergy is on the Rise

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Abbreviations:

NADPH = reduced nicotinamide adenine diphosphate
SOD = superoxide dismutase

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Abstract:

Latex is produced from the *Hevea brasiliensis* tree. It has many uses in medical devices and everyday articles. Latex allergy incidence has been increasing as the prevalence of this allergen increases in the environment. The allergic response involves IgE and mast cells. During this reaction IgE stimulates monocytes and macrophages to produce superoxide. Superoxide can be used to kill the foreign organism and to stimulate a larger immune response. Latex proteins have homology to many known proteins including superoxide dismutase. The latex SOD can interfere with the normal immune response, disrupting the redox status and causing more damage. It has been shown that allergic patients have significantly higher levels of IgE in their plasma. Treatment for this allergy includes avoidance and immunotherapy, with avoidance being the safest. This paper will briefly explain the production and structure of latex, allergic reaction to latex, and reactive oxygen production.

Introduction

Latex is widely used in medical devices, like syringes and tubing, as well as everyday articles like paint and adhesives. The prevalence of allergies to latex in the general population is in the range of 2.9 to 17% [1]. Prevalence depends on time of exposure and the concentration of the latex allergens in the environment. An environment where the concentration of latex allergen is both low and high is in hospitals. Latex allergens in surgical areas have been determined to be 10 to 100 fold higher than in non-surgical areas. The high concentration of latex particles can lead to increased sensitization of health care personnel and patients.

There are people that have a sensitivity to latex without repeated exposure. One such group is spina bifida patients, where 18 to 65% are allergic to latex [1]. The allergy is determined by the presence of immunoglobulin E (IgE) serum antibody and symptoms with latex contact.

The majority of the latex used commercially comes from *Hevea brasiliensis* [1]. Latex contains lipids, carbohydrates, proteins and many inorganic constituents including potassium, magnesium, calcium, sodium, zinc, manganese, copper and iron [2]. Latex protein content varies from 1 to 1.8% [2]. The number of individual proteins in latex is more than 200, however hevein and hevamine make up the majority [3].

Not all of the proteins from latex can induce an allergic response. The proteins that can induce a response are able to bind IgE to some extent [2]. Some of these immunoreactive proteins show a high degree of homology to known proteins. The homology includes proteins like enolase, superoxide dismutase, triosephosphate isomerase, proteosome subunit and chitinase [3].

This paper will briefly explain the production and structure of latex, allergic reaction to latex, and reactive oxygen production.

Production of Natural Latex

Natural rubber is produced commercially from the latex of the *Hevea brasiliensis* tree that is cultivated in plantations mainly in the tropical regions in southeast Asia [2]. Natural rubber is a milky liquid known as latex, which is a suspension of very small particles of rubber. Liquid latex is collected from the trees, diluted to about 15% rubber content and coagulated with formic acid [2]. The coagulated material is then compressed through rollers to remove water and to produce a sheet material. Rolled sheets are usually further compressed to break up some of the long polymer chains, this reduces the average molecular weight and makes it easier to manipulate.

Structure of Natural Latex

Natural rubber is mainly composed of linked units of cis-1,4 isoprene mixed with small amounts of proteins, lipids and inorganic salts [2]. cis-1,4 Polyisoprene is a long chain of subunits with an average molecular weight of 5×10^5 gm/mol [2].

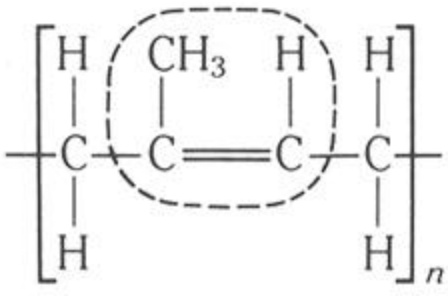

Figure 1: Structure of cis-1,4 polyisoprene [2]

Polymer chains of natural rubber are long, entangled and coiled. At room temperature the chains are in a constant state of agitation, this is from the steric hindrance between the methyl group and the hydrogen atom located on the same side of the carbon-carbon double bond [2]. Arrangement of the covalent bonds in the natural rubber polymer chain is seen below in figure 2 [2].

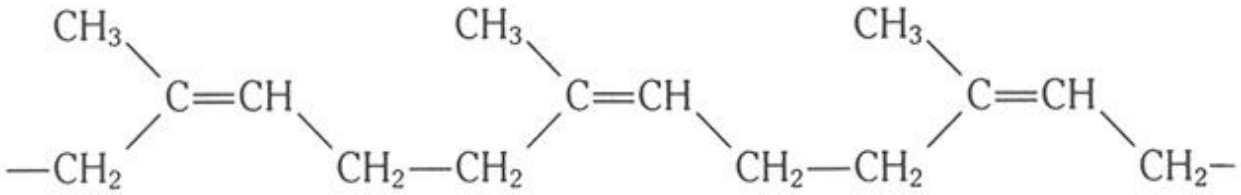

Figure 2: Segment of natural rubber polymer chain [2]

Synthetic Latex

The most common synthetic rubber is nitrile. Nitrile rubbers are copolymers of butadiene and acrylonitrile with proportions ranging from 55 to 82% butadiene and 45 to 18% acrylonitrile [2].

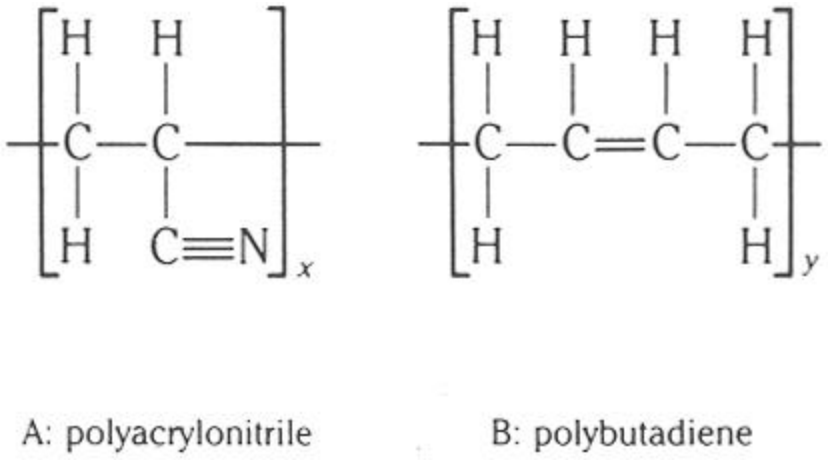

Figure 3: Monomer of polybutadiene and polyacrylonitrile [2]

There are several drawbacks to the synthetic latex, molecular flexibility is reduced and cost is higher than natural latex.

Diagnosis and Treatment of Latex Allergy

Development of a latex allergy results from the exposure to antigens by cutaneous, mucosal and parenteral routes [1]. Diagnosis depends on IgE/mast cell controlled reactions that include redness, itching or swelling after contact with latex products or unexplained episodes of hives [1]. Skin tests with latex allergens either from crude natural rubber latex or from extracts of latex products may be helpful. However most crude preparations are not consistent because of the complexity of the solution with antigens in both the liquid and solid phase [1].

Treatment of latex allergy follows the same course as for other allergies, avoidance and immunotherapy. Immunotherapy produces blocking antibodies and favors the transformation of lymphocytes T helper 2 (TH2) into T helper 1 that are unable to stimulate the mast cell [4]. Immunotherapy also stimulates the increased production of interferon gamma (IFN-?) which can inhibit B lymphocyte production of IgE [4].

IgE and mast cells

The IgE response is a local event occurring at the site of the allergen's entry in to the body. IgE production by B cells involves antigen presentation by antigen presentation cells, T cell help and stimulation of B cells to produce IgE [5]. The first IgE produced will sensitize local mast cells. The excess IgE will enter the circulation and bind to receptors on both circulating basophils and tissue fixed mast cells throughout the body [5]. Levels of IgE have been shown to be higher in allergic patients than in controls. Mean serum IgE concentration is 224 IU/mL in allergic asthma and 43 IU/mL in controls [5].

IgE stimulates Superoxide production

Allergic diseases have a common biologic characteristic of developing an IgE immune response to low concentration of allergens. Cells infiltrating the airways and cells circulating in the blood stream express low affinity IgE receptors on their surfaces. These cells can be stimulated by IgE dependent mechanisms, releasing lysosomal enzymes, eicosanoids, cytokines and superoxide [6]. Peripheral blood monocytes have been shown to reduce oxygen first to superoxide (by reduced NADPH oxidase) and then to hydrogen peroxide (by superoxide dismutase) when appropriately stimulated [6]. Hydrogen peroxide is then either transformed by myeloperoxidase into hypochlorous acid or hydroxyl radical (through the Iron catalyzed Fenton reaction) [6].

Comparison of low affinity IgE receptor (CD23) expression versus serum IgE induced superoxide production showed a linear correlation ($r = 0.92$) [6]. This correlation indicates that higher levels of receptors correspond to a higher sensitivity to IgE. Increased sensitivity to IgE could then lead to a larger and more severe inflammatory response [6].

When monocytes, isolated from people with allergies, were exposed to IgE there was a significant increase in the production of superoxide [6]. Furthermore, this production did not peak until after the monocytes from normal individuals had already returned to baseline [6]. When anti-IgE antibodies were added, the superoxide release could be completely blocked [6].

Characterization and identification of latex allergens show that some of the IgE reactive protein spots (from a 2d gel) have high homology with SOD [3]. Latex SOD can dismute the superoxide, interfering with the ability to mount an effective immune response. For the body to

then react to the foreign material more cells, monocytes and macrophages, are recruited to produce more reactive oxygen. Active oxygen becomes toxic when an imbalance arises between antioxidant enzymes and free radical production during an allergic reaction. Free radical production and disturbance in redox status can then modulate the expression of a variety of immune and inflammatory molecules. This modulation leads to inflammatory processes, both exacerbating inflammation and effecting tissue damage. Abnormal immunity has been related to oxidative imbalance and immunosuppression. The immunosuppressive response can then lead to higher levels of cell recruitment, reactive oxygen production and damage. So that each time a sensitized person encounters the antigen, more and more damage can occur.

Characteristic blood biochemical features of asthma are excessive superoxide and hydroxyl radical production and reduced free radical scavengers in blood cells and antioxidant deficiency [7]. There is also a higher lipid peroxidation product in plasma, cell and cell membrane [7].

Conclusion:

Latex allergies can develop when a person is exposed to latex. Allergens interact with the immune system to produce IgE. IgE can activate monocytes to release lysosomal enzymes, cytokines and superoxide. Superoxide is used to kill the foreign invader and stimulate a larger immune response. There are latex proteins that have a strong homology to SOD. The latex SOD can interfere with an immune response. The interference can then cause the body to recruit more cells to produce more superoxide. High levels of superoxide can disrupt the redox status and suppress the immune system. This modulation can lead to higher levels of inflammation and

tissue damage. Latex allergies can be treated with immunotherapy or avoidance. Immunotherapy looks promising but it can interfere with the normal response to pathogen. Avoidance is the safest answer to this complex problem but unfortunately is not sufficient as latex use increases. Hopefully in the future a material will be developed that has all of the benefits of latex without the immunologically active components.

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