906 LATEX ALLERGY IN THE WORKPLACE.

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The United States Occupational Safety and Health Administration (OSHA) estimates that 8-12% of healthcare workers are sensitized to natural-rubber latex. In addition, approximately 0.5-1% of the general population is reported to be sensitized. Clinical signs and symptoms of latex induced disease range from simple irritation to immunologic manifestations such as urticaria, asthma, and anaphylaxis. The mechanisms of latex allergy are complex, and are induced by exposure to numerous allergenic proteins found in natural-rubber latex as well as other chemicals used in latex products manufacturing. For example, there are 250+ proteins containing multiple epitopes in latex of which at least 30 have allergenic potential. Several latex proteins have been epitope mapped. Sequencing demonstrates both unique epitopes and sequences commonly found in other plant proteins. These common epitopes result in cross-reactivity to other plant allergens found in pollens and foods. A further complication arises from the ability of latex proteins to associate with glove powder. This enhances the potential for respiratory sensitization from aerosolized powder associated proteins, and both humans and experimental animals have demonstrated hypersensitivity following exposure to latex via the respiratory route. The diagnosis of latex allergy is complicated by these variables, which in turn hinders the development of intervention strategies. Further epidemiological assessment can more explicitly define the scope, trends, and demographics of latex allergy. Diagnostic accuracy can be improved through greater knowledge of proteins involved in the development of latex allergy, and factors analysis of presently available diagnostic tests. *In vivo* and *in vitro* models can elucidate mechanisms of sensitization and provide an understanding of the role of exposure route in latex associated diseases. Combined, these efforts can lead to intervention strategies for reducing latex allergy in the workplace.

907 LATEX ALLERGY: CLINICAL AND EPIDEMIOLOGICAL DATA.

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Natural rubber latex (NRL) allergy has become an important occupational health concern particularly among healthcare workers (HCWs). Clinical manifestations include irritant contact dermatitis, allergic contact dermatitis (type 4), and type 1 immediate hypersensitivity responses. Type 1 (IgE mediated) NRL allergy includes contact urticaria, systemic urticaria, angioedema, rhinitis, conjunctivitis, bronchospasm and anaphylaxis. Diagnosis of type 1 latex allergy is made by accurate history including questions on atopic status, food allergy, reactions to latex devices (gloves, balloons, condoms), and reactions during medical and dental procedures. To confirm a diagnosis either *in vivo* skin prick testing (SPT) or *in vitro* assays for latex specific IgE are performed. The major source of workplace exposure has been the powdered NRL gloves used by HCWs. Surveys of HCWs have demonstrated that the prevalence of sensitization to latex ranges from 2.9% in Finland to 4.7% in Belgium among hospital workers as a group, and from 6.2% in operating room staff in Finland to 9-10% in Canada and France. We recently observed that the prevalence of latex sensitization based on SPT was 12.1% with a minimum prevalence of 9.5% among 1351 HCWs in two hospitals. There were significant associations with atopic status, positive SPT to certain foods, work related symptoms, and departmental use of gloves per HCW. In this study about 60% of the latex SPT positive participants had work related symptoms. It has been reported that 2.5% of HCWs have latex induced occupational asthma confirmed by specific inhalational challenge. Sensitization to latex has extensive cross-reactivity with certain foods and leads to clinical allergic reactions. Positive food SPTs occurred in our patients with the following frequency: avocado (53%), potato (40%), banana (38%), tomato (28%), chestnut (28%), and kiwi (17%). As well we reported that dental school students were at high risk for latex sensitization with prevalence rates of 0% for year one and two students, 6% of year 2 students, and 10% of year four students having a positive latex SPT. The prevalence of latex sensitization in occupationally unexposed groups is quite low, generally less than 1%.

908 MOLECULAR CHARACTERIZATION OF LATEX ALLERGENS.

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Type 1 latex allergy is an IgE mediated response to antigenic proteins found on products made from natural rubber latex. Natural rubber latex is harvested from trees and ammoniated to prevent coagulation resulting in the hydrolysis of the latex proteins. Prior to use in manufacturing, the latex is formulated by the addition of multiple chemicals. Thus, human exposure is to a mixture of residual chemicals and hydrolyzed latex peptides. The hydrolyzed nature of the allergens has complicated identification of major allergens and the development of reagents for *in vivo* and *in vitro* diagnostic tests. Multiple investigators, using a variety of methodologies, have succeeded in identifying the major IgE binding allergens (Hev b 1-8). More recently, these proteins have been cloned, sequenced and expressed as recombinant proteins. Skin testing with recombinant Hev b 2, 3, 5, 6, 7, and 8 revealed Hev b 5, 6 and 7 to be the most common allergens for healthcare workers. Using overlapping synthetic peptides, IgE binding epitopes have been determined for these allergens. Hev b 5 contained at least 6 epitopes, while Hev b 7 contained 12 epitopes all with limited sequence homology to other known plant proteins. Hev b 6 however, contained six epitopes with sequence homology to defense proteins common to many different plants. Sequence homology helps to explain the cross reactivity to a variety of foods experienced by latex allergic individuals. The development of recombinant allergens provides reagents which should greatly improve the diagnostic accuracy of tests for latex allergy.

909 COMPLICATIONS IN INTERPRETATION OF DIAGNOSTIC TESTS FOR LATEX ALLERGY.

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The diagnosis of natural rubber latex allergy begins with a clinical history and often involves a confirmatory test. While the puncture skin test (PST) has been regarded as a primary confirmatory test for the assessment of patients for IgE-mediated disease, the absence of an FDA-licensed Hevea brasiliensis latex extract in the USA has restricted its use in the diagnosis of latex allergy. Serological tests have therefore become critically important as alternative diagnostic tools. Three manufacturers have currently obtained 510K clearance from the FDA for their latex *in vitro* reagents: the CAP System (Pharmacia-UpJohn); the AlaSTAT, (Diagnostic Products Corporation) and the HY-TEC assay (HYCOR Biomedical). Although all of these commercial assays are based on non-ammoniated latex (NAL) as their primary allergen, there are differences in their solid or soluble supports and detector systems. Paired-comparisons of the three assays indicates that they disagree on the antibody status of an individual serum. This leads to patient's sera being "positive" by one or two tests and negative in (an)other(s). It is speculated that the disagreement among tests is due to IgE antibody assays detecting different subsets of IgE antibody of a given specificity, possibly as a result of differential specificities of their allergen-containing reagents. Reasons for this include variability in allergen content in different batches of source latex; sensitized individuals producing specific IgE antibody to at least 8 *Hevea* allergens, Hev b 1-Hev b 8, each of which differs in its structure, size, net charge (pI), relative allergenicity and abundance in natural rubber latex. The relative content and ratios of Hevs in the final allergen preparation most probably could enhance the diagnostic accuracy of a specific test. Other potential causes of allergen-containing reagent heterogeneity include variable stability during storage and variable binding of allergen to labels (e.g., biotinylated co-polymer in AlaSTAT) or solid supports (sponge in CAP; cellulose disc in HYTEC). Using receiver operating characteristic (ROC) curve analysis, and positive PST to NAL as the discriminator, the HY-TEC system has significantly greater ($P<0.01$) area under the curve (AUC, 0.924 + 0.017, standard error) than CAP (0.869 + 0.024) or AlaSTAT (0.858 + 0.024), suggesting it may be more accurate under the comparison conditions evaluated.

910 ANIMAL MODELS AND MECHANISMS OF LATEX ALLERGY.

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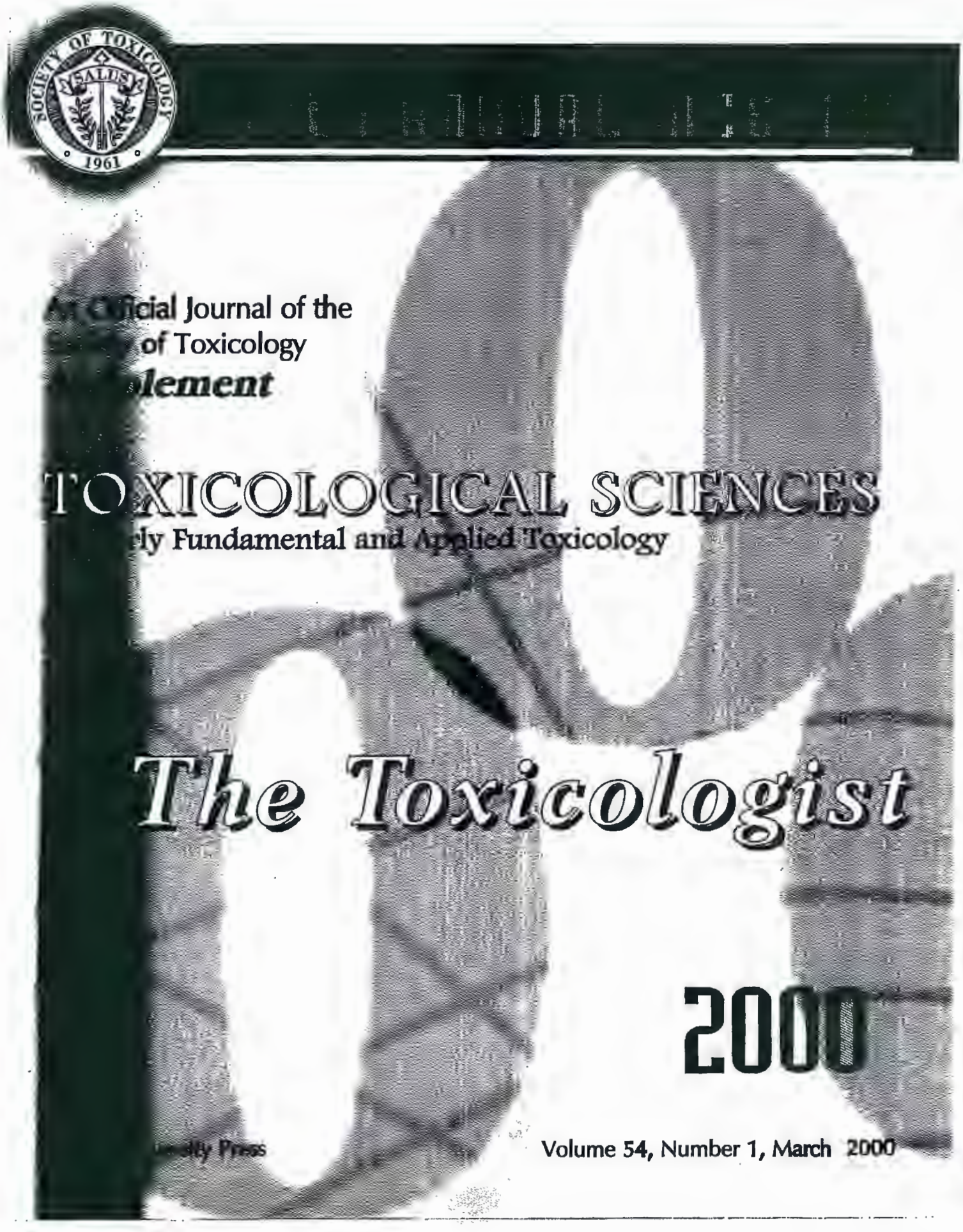
Animal models are frequently used to conduct mechanistic studies that due to test article toxicity or sensitization potential would be unethical to perform in humans. Several laboratories have developed models to study latex allergy and although these include rabbit and guinea pig models, most animal research has been conducted in murine models. Although clinical and exposure data have been gathered on the factors affecting the elicitation of responses in latex allergic individuals, less is known regarding the development of sensitization. Coupled with *in vitro* dermal penetration studies, murine models were established to investigate the role of the route of exposure in the development of latex sensitization. Time course and dose response



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