

POSITION PAPER

Latex allergy. A position paper of the British Society of Allergy and Clinical Immunology

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Introduction

This document is intended to be a measured response to concerns over latex allergy. It is not intended to be an exhaustive summary of the extensive literature, but we believe we have included all important data and have endeavoured to support all statements with published evidence. Where possible we have made specific reference to UK data, although these are curiously few.

The document should be of interest to allergists, occupational health professionals and others who treat patients with established or suspected latex allergy. Without apology, it begins with a lengthy description of rubber manufacture, which we believe will clarify many common misunderstandings and provide a firm setting for subsequent sections. Immunological, clinical and epidemiological summaries are followed by sections on allergic, contact dermatitis, and the special issues relating to urological, dental and anaesthetic practice. The final paragraphs are concerned with occupational health issues and primary prevention.

Two types of allergic responses to latex are distinguished: 'immediate-type' responses (Type I), associated with the production of specific IgE antibodies, which begin shortly after allergen exposure although their effects (particularly asthmatic) may persist for much longer; and 'delayed-type' hypersensitivity responses (Type IV) which have a longer latency and are not associated with IgE antibodies.

Manufacture and chemistry of natural rubber (NR) and associated products

Rubber

NR, a 1:4 *cis*-polymer of isoprene (molecular weight $0.15 - 2 \times 10^6$ Da), satisfies about 25% of the world elastomer demand. Other high molecular weight, naturally occurring polyisoprenoids are *trans*-polyisoprenes found in gutta percha and balata and a mixture of *cis*- and *trans*-polyisoprenes found in chicle, an original constituent of chewing gum. Synthetic rubbers include styrene butadiene (SB), polychlorobutadiene (neoprene), acrylonitrilebutadiene (nitrile rubber

– (NB)), styrene ethylene butadiene (SEB), polyurethane and synthetic polyisoprene rubbers.

The commercial rubber tree *Hevea brasiliensis*, a member of the family *Euphorbiaceae* (spurges) and an erstwhile native of the Amazon basin but now grown commercially in SE Asia and West Africa, should not be confused with the domestic 'rubber plant' *Ficus elastica* or its close relative the 'weeping fig' (*Ficus benjamina*) each of which has also been implicated in allergic responses.

Production of NR latex

The lactifers of *H. brasiliensis* are subject to a diurnal variation in turgor pressure that is highest about midnight. This allows the release of *c.* 200 mL of latex over 1–2 h when a half spiral cut is made at the base of the tree in the early morning. Latex productivity has been increased by selective breeding and by hormone treatment of trees; both the latter and regular tapping are likely to increase the formation of the so-called pathogenicity-related proteins of latex exemplified by hevein, chitinase and β -1,3-glucanase [1].

Tapped latex contains about 25–30% rubber in the form of 50–3000 nm diameter globules bounded by a half unit membrane composed largely of phosphatidyl choline. In this are embedded several polypeptides, the chief of which is the 14.5 kDa 'rubber elongation factor'. Latex also contains a number of organelles and, in particular the highly osmosensitive luteoid which combines the functions of a tonoplast and a lysosome. This contains a number of basic proteins, in particular the β -1,3-glucanase and chitinase/lysozyme enzymes, which in addition to the acidic luteoid-protein hevein have allergenic activity.

Dry rubber production

About 90% of latex obtained by alternate daily tapping is destined for the production of 'dry rubber goods' where frequently, as in the case of vehicle tyres, it will be used together with synthetic elastomers such as SB. Latex for this purpose is collected about 2 h after tapping and transported to a nearby factory where it is diluted to give a rubber content of about 15% and the pH is adjusted to about 4.5 with formic or acetic acid. Following the reduction in charge on the rubber particles, the latex coagulates; this coagulum is allowed to stand for an hour or two, after which it is washed. The crumbs of coagulum are then passed between rollers and heated to 60 °C after which the sheets are dried for up to a

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Table 1. Uses of natural rubber

Bulk (dry) natural rubber	%	Latex concentrate	%
Tyres	70	Gloves	40
Latex goods	12	Adhesives	16
Shoes	5	Thread	12
Engineering	3	Foam	12
Cables and tubes	2.5	Carpets	7
Vehicles	1.5	Imitation leather	7
Other	6	Other	6

week in a smoke house, resulting in the ribbed smoked sheet of commerce. Alternatively, the washed crumbs of coagulum may simply be dried in air at 100–130 °C, after which they are compressed into bales. A lower grade of rubber is 'cup lump' in which the latex has been allowed to coagulate overnight as a result of the combined actions of indigenous latex enzymes and bacterial attack.

Various chemicals may be added to latex prior to coagulation. Among these are: castor oil to facilitate crumb formation, sodium metabisulphite to inhibit browning, and hydroxylamine to diminish any increase in rubber viscosity during storage. Dry rubber contains about 94% rubber, 2% protein and 3% carbohydrate [2, 3].

Manufacture of articles from dry rubber involves an initial mastication, causing the formation of free radicals, during which a plasticizer, vulcanizing agents (commonly sulphur), accelerators such as thiurams, thiazoles or dithiocarbamates and activators such as zinc oxide together with stearic acid and carbon black as a filler are added. The masticated rubber is then extruded through a die, calendered between rolls (e.g. for conveyor belt production) or moulded as for vehicle tyres. The formed articles are then vulcanized by heating to about 140 °C, giving an elastic product of reduced tackiness and low solvent solubility (Table 1).

Allergenicity of dry rubber

Whilst the low-molecular-weight additives incorporated in dry or black rubber have long been known to be a cause of Type IV hypersensitivity, the possibility that the protein component of such materials (about 2% of the mass) can excite an immediate or Type I hypersensitivity cannot be precluded. Although aircraft tyres contain a considerable amount of NR, the tyres of cars and heavy vehicles, which are subject to multiple retreading, have very little NR in the wearing tread [4]. Nevertheless evidence for the presence of *cis*-polyisoprene in particles present in urban air was obtained by Williams et al. [5]. An extract of similar particles has been shown to inhibit a latex specific human IgE assay and to contain a 34–36 kDa polypeptide reacting with the IgE of latex-sensitive individuals in immunoblots [6]. However, total amino-acid analysis of the aqueous extract of natural dry rubber crumb (as used for car tyres) revealed only 0.23 p.p.m. protein, less than one-thousandth of that found in high-quality surgeons' gloves [7]. Nonetheless, this protein extract was antigenic; 3/13 latex-sensitive patients gave a positive skin prick test when challenged with a 10 µg/mL solution.

Production of latex concentrate

The remaining 10% of tapped latex is used for the production of directly prepared goods. In this case, tapped latex is immediately stabilized by the addition of 0.25% ammonia. This 'field latex' is transported to a factory where its rubber content is enriched by centrifugation; a cream of rubber separates from a lower skim layer. The latex concentrate to be used for particular purposes, such as the production of condoms or electricians' gloves, may be diluted with water and recentrifuged to give a preparation of lower protein content. Normal concentrate contains about 1% protein in addition to 60% rubber. The proteins of the latex organelles are released into the serum during processing. After centrifuging, the ammonia concentration is usually increased to 0.7% giving a pH of 10.6 – high-ammonia latex (HAL). However, to avert some of the problems and unpleasantness of using a liquid with such a high concentration of ammonia, an alternative low-ammonia (LA) stabilization system has been developed using 0.2% ammonia together with 0.025% of a 1:1 mixture of tetramethylthiuram disulphide (TMTD) and zinc oxide to give LA-TZ latex. Low-ammonia latex preserved with boric acid (LA-BA) may be preferred for light-coloured objects such as babies' teats and pacifiers [8].

After centrifuging and ammoniation, the latex is stored for a month at ambient temperatures of around 30 °C. The physical result of this ageing is an increase in mechanical stability which is correlated with the capacity to form a stable film on dipping. The HAL is then passed to the manufacturer which in the case of export to Europe or the US involves container transport by sea during which the latex may reach temperatures in excess of 40 °C. Thus, whilst 4–6 weeks may have elapsed before HAL is used for manufacture in SE Asia, 5–12 months may elapse before it is used in the US or Europe. This may have some bearing on the final allergenicity of the product [9].

Nowadays, most latex concentrate is used for the production of dipped latex goods. However, in the 1960s and 1970s, a significant amount was used for the production of articles such as foam-rubber mattresses. Modern latex foam is based on blends of natural and SB rubbers and is used in upholstery, bedding and seals (particularly in vehicles). Latex is also used extensively in the manufacture of adhesives.

Unvulcanized ammoniated latex concentrates are prepared for use in dipping by the addition of a vulcanizing agent, usually sulphur or a sulphur donor together with an accelerator such as zinc diethyl or dibenzylthiocarbamate. Vulcanization may be activated by the addition of zinc oxide. Occasionally, the milk protein, casein, or gelatin may also be added [10].

For the formation of a rubber film, a thoroughly cleaned former is essential. Chromic acid is often used as the cleaning agent. The former is then coated with a coagulant, usually calcium nitrate, together with mould release agents such as stearate, calcium carbonate or cornstarch and a surfactant such as potassium dodecyl sulphate. The precise composition of the coagulant determines the thickness of the subsequently formed film. The dried former is then dipped in the prepared latex for a specified dwell time. The coagulated gel which has adhered to the former may then be wet-leached to remove proteins, salts and surfactants; alternatively, the gel may be

dried before leaching. Pre-powdered gloves are subsequently treated with cornstarch, whilst some non-powdered gloves are dipped in a coating polymer (usually containing hydroxyethyl methacrylate). The dried, leached gloves then pass to a vulcanizing oven where the temperature rises to 150 °C, during which much of the remaining protein is brought to the surface where it may be absorbed by cornstarch. There then may follow a further dry leach and, in the case of powdered gloves, further application of cornstarch. Household gloves usually, and surgical gloves occasionally, are then finally chlorinated by treatment with, for example, sodium hypochlorite in the presence of acid.

Surgical gloves are sterilized usually by irradiation. Ethylene oxide gas may be used as an alternative but latex proteins can become more allergenic as a result and ethylene itself may act as a hapten.

Problems with latex gloves

The necessity to lubricate gloves to facilitate donning has always been a source of problems. The original use of talc in surgical gloves was abandoned in the 1950s on account of its role in the induction of post-operative granulomata and adhesions. Some latex proteins tend to be adsorbed by high-molecular-weight polysaccharides; repeated donning and removal of gloves in the theatre preparation room can generate an atmosphere heavy with protein-charged cornstarch particles [11]. Furthermore, the cornstarch slurry into which the gloves may be dipped during production is a highly favourable environment for bacterial growth. Although the bacteria themselves are subsequently killed on sterilization, endotoxic cell-wall lipopolysaccharides from Gram-negative organisms may persist to cause dermatitis in the wearer [12]. There is also some evidence that starch powder may itself be immunogenic [13]. The potential allergenicity of gloves is usually assumed to be related to the total extractable protein which may vary from 50 to 500 µg/g of glove (1 g of glove corresponds to approximately 50 cm² of an average surgeon's glove). The current methods of protein determination, however, present problems [14]. The eluate of latex gloves appears to be composed largely of proteins of molecular weight greater than 14 kDa and there does not seem to be much evidence for the presence of the reported low-molecular-weight allergens, hevein and the rubber elongation factor.

Notwithstanding their disadvantages, NR gloves are preferred by surgeons and other users when compared with their synthetic competitors (see Table 2) on grounds of their impermeability to small viruses, their excellent elasticity and their low cost.

NR in other medical and household devices

Urinary catheters are made entirely of NR and the surface allergens may be particularly significant in sensitizing patients with spina bifida. Plungers may contain some NR together with butyl rubber but closures such as vial bungs are usually made of butyl rubber (Table 3a and b).

Table 2. Gloves and condoms made from synthetic rubbers

Material	Gloves	Manufacturer
Neoprene	Biogel Neo-tech	Regent
	Duraprene	Baxter
	Dermaprene	Ansell
	Neolon	Maxxim
	Elastyren	Herdal
SBR	Tactyl 1	Smart Practise
SEBR	Synthesis	Smart Practise
	Allergard	Johnson & Johnson
<i>Condoms</i>		
Polyurethane	Avanti	SSL International

Table 3.

(a) *Some common medical devices, other than gloves, that may contain latex*

Bite blocks
Blood pressure cuffs
Bulb syringes
Catheters*
Dental coffer dams*
Elastic bandages
Electrode pads
Endotracheal tubes and airways
Enema syringes*
Ventriculo-peritoneal shunts
Finger cots
IV access injection ports
Manual resuscitators
Penrose surgical drains
Pulse oximeters
Stethoscope tubing
Stretcher mattresses
Tourniquets
Vascular stockings

(b) *Some household goods that may contain latex*

Adhesives
Balloons*
Carpet backing
Condoms*
Contraceptive diaphragms
Elasticated fabrics*
Feeding nipples
Household gloves*
Diapers and incontinence pads
Infant pacifiers
Rubber bands
Shoes

*Reported as sources of allergenic sensitivity.

Immunology of latex

Latex contains over 200 polypeptides [15], and identifying allergens within it has been a considerable task of the last decade (see Table 4). Most immunoclinical studies of latex sensitization or allergy have examined one of two high-risk groups: health-care workers and patients with congenital urological abnormalities. The former are believed to be

Table 4. Natural rubber latex allergens

Systematic name	Conventional name	MW (kDa)	Notes*
Hev b1	Rubber elongation factor	14.6	80% SB 50% HCW
Hev b2	β -1,3-Glucanase	34–36	Minor allergen
Hev b3	Rubber particle protein	23	80% SB, 20%HCW
Hev b4	Microhelix protein complex	100–115	Minor allergen
Hev b5	Acidic C-serum protein	16	92% HCW, 56% SB
Hev b6	Prohevein	20	
Hev b6.01	Hevein	4.7	80% HCW, 70% CH
Hev b6.02	Prohevein C-domain	14	30% SB, 33% CH
Hev b7	Patatin-like protein	46	Minor allergen

*SB, patients with spina bifida. HCW, health-care workers.

exposed through inhalation of airborne allergens released from (powdered) latex gloves, or through wearing latex gloves [16]. Patients with spina bifida and other surgically treated congenital malformations are exposed to latex through contact with surgeons' gloves during multiple operations and through the presence of indwelling latex medical devices. Latex allergens recognized by each group may be distinct; health-care workers predominantly recognize water-soluble proteins from the lutoid fraction, whereas spina bifida children recognize hydrophobic proteins normally found tightly bound on rubber particles. Differences in the pattern of allergen binding may result from different routes of latex exposure although this remains speculative. Children sensitized to latex who have not undergone any surgical procedures have a pattern of IgE reactivity which resembles that of health-care workers [17].

Major allergens for patients with spina bifida

Hev b1 and Hev b3, hydrophobic proteins found tightly bound to rubber particles, appear to be the major latex allergens for the spina bifida group [18, 19]. The allergenic regions of Hev b1, a 14.6 kDa protein known as rubber elongation factor reside within the C-terminus and within amino acids 31–64. Comparisons of the sequences of Hev b1 against protein sequence databases do not reveal any similarities with other proteins. Hev b1 is recognized by 80% of sensitized spina bifida patients but also by 50% of health-care workers [20].

Hev b3 is a 23–27-kDa protein, which fragments easily into several polypeptides of lower molecular weight. It has sequence similarities with Hev b1 and is recognized by 80% of the spina bifida group but only 20% of health-care workers [18, 19].

Major allergens for health-care workers

Hev b6.02, a 4.7 kDa N-terminal fragment of prohevein (Hev b6.01) belongs to the group of Class I chitinases, which accumulate in plants in response to stressful conditions and serve to protect them from attack by a wide range of pathogens. Hev b6.02 is the major allergen of health-care

workers and latex-sensitized children who have not undergone surgical procedures, and is recognized by 80% and 70% of these groups, respectively. Hev b6.02 is also recognized by 30% of the spina bifida group and 33% of children who have undergone surgical procedures [17, 21].

Hev b5, another allergen recognized by health-care workers (and about half of patients with spina bifida) [22], is a 16 kDa (possibly cytoplasmic structural) protein, which has high sequence homology with a protein from kiwi fruit termed pKIWI501 [22, 23]. This polypeptide appears in the early stage of fruit development, but its biological function is unknown. Ninety-two per cent of health-care workers and 56% of spina bifida patients recognize Hev b5 [22].

Other minor allergens recognized by latex-sensitized patients are Hev b2, 4 and 7, heveamine, Mn-superoxide dismutase, enolase, profilin, lysozyme and papain [18]. Hev b7 has a dual role as a somatic storage protein and as an enzyme involved in host resistance. Its sequence is homologous to patatin storage proteins encoded by a multigene family found in plant families such as potato and yeast [24]. Hev b2 belongs to a group of defence-related enzymes synthesized by plants in response to microbial and fungal infection. Mn-superoxide dismutase and enolase are well-conserved proteins and have been described as important allergens in mould [19].

It is striking that the majority of allergens recognized by latex-sensitized patients belong to pathogenesis-defence related proteins. The current epidemic of latex sensitization may have been precipitated by an increase in demand for latex products in the early 1980s. Possibly, this led to greater stress on rubber trees with increased use of yield stimulants, more frequent tapping of rubber trees and the accumulation of hevein [25, 26].

Latex and fruit allergies

Almost half of latex-sensitized patients display an associated fruit allergy, most commonly to avocado, banana and kiwi, but also to other species including nuts. Endochitinases belonging to the same group as Hev b6.02 have been identified as cross-reacting allergens in avocado and chestnut [27, 28], banana [29] and sweet pepper [30]. Other latex allergens such as Hev b5 are known to have sequence homologies with kiwi fruit [22, 23], and Hev b7 with patatins found in tomatoes and potatoes [24, 26]. Some fruit-associated latex sensitization may be due to common allergens, possibly plant defence-related proteins, found both in latex and fruits; in other cases it probably reflects the broad allergic repertoire of some individuals, particularly children.

Epidemiology

Introduction

Latex 'sensitization' or 'sensitivity' may usefully be defined as the presence of a positive skin prick test to latex allergens or the demonstration of specific IgE antibodies in serum. Latex 'allergy' describes the elicitation of immediate-type allergic symptoms by contact with latex in a sensitized individual. The difficulty in identifying these phenotypes separately, and in

relation to each other, hampers a clear understanding of the epidemiology of adverse reactions to latex. On the one hand, immunological techniques for defining sensitization may be of doubtful specificity and reliability. Equally, the current methods for detecting symptoms consistent with latex allergy are unstandardized and do not easily distinguish the different types of immune (or irritant) reactions to rubber.

Prevalence

The apparent epidemic of the disease can be dated to the early 1980s [31]. In the 20 years since the first, modern description of latex urticaria, Medline records over 150 articles on the prevalence of latex 'allergy', all but one published in the last 10 years. It is unclear to what extent this reflects the natural enthusiasm among allergists (and editors) for a novel allergen, or better recognition of what is really an older problem. The clinical features of latex allergy, however, are generally distinct enough to suggest that it is a problem that would have been difficult to 'miss' entirely, and there is of course at least one plausible explanation for a truly epidemic pattern. Nonetheless, it remains a fact that there is little firm evidence to support this. The great majority of published studies are either small, cross-sectional surveys conducted within populations believed to be at high risk, or uncontrolled case series. There are very few studies of incidence, and none that measures incidence rates across time. The dramatic increase in reported cases over recent years seems likely to reflect in part the accumulation and ascertainment of prevalent cases rather than necessarily a steep rise in incidence.

Studies in this area fall into two groups: the majority examine latex sensitization or allergy (or both) in high-risk occupational populations (health-care workers in particular) or patient groups (those with congenital urinary dysfunction). Less frequently, the same outcomes have been examined among patients attending allergy clinics. Alternatively, but less often, the prevalence of latex sensitization among the wider population has been estimated, usually by assay of serum-specific IgE antibodies. It is not our purpose to review this literature exhaustively but below we summarize some important features.

'General' populations As proxies for general populations, four studies have estimated the frequency of latex-specific IgE

antibodies among blood donors [32–35]. A further study has examined a representative US adult population [36]. It should be noted that diagnostic tests with imperfect specificity tend to overestimate (sometimes very considerably) the prevalence of disease when the true frequency is low [37]. Although the mean ages in each blood donor population were similar, the disparities in their sex distributions (Table 5) neatly demonstrate the hazards of assuming that such populations are genuinely representative. In two [33, 35], health-care workers were excluded from the analyses. Different immunoassays were used in the studies but some rough comparisons may be made. With the exception of the recent US study [36], the frequencies of latex-specific IgE antibodies were low. In two surveys [32, 33], men were more likely than women to have specific antibodies; in the third [34], the reverse was true. Merrett reported a decreasing prevalence of antibodies with increasing age; this pattern was not evident in the other surveys. Overall however, there is a striking concordance in the results from the blood donor surveys. Such close agreement raises the possibility that the assays used are not wholly specific for latex and that positive responses may, to an uncertain degree, indicate sensitization to one or more immunologically similar antigens.

Very similar, too, are the findings from a survey of 20–40-year olds attending a health screening service in France [38]; only 34% of the eligible population were surveyed. This, and the study of Senna et al. [35], included also skin prick testing with a commercial latex extract; in the French population, no individuals had both positive RAST and skin prick tests. In contrast, each of the six donors with a Class 3 CAP to latex in the study of Senna et al. had positive skin prick tests to latex; only one however reported symptoms provoked by latex contact.

Alternative approaches have examined other purportedly representative populations. Turjanmaa et al. [39] reported, in anecdotal form, 183 cases of clinical latex allergy attending either of two allergy clinics servicing a total population of 430 000 in Finland, approximating to a minimum prevalence of 0.04%. The age distribution of the clinic catchment populations was not stated. Pre-operative skin prick testing with a latex glove eluate in 804 consecutive patients at one of the hospitals produced a single positive result only (0.12%).

Table 5. Prevalence estimates of latex sensitization in 'general populations'

Author (ref)	Source population	#	Male	Mean age	Immuno-assay	+ latex IgE (%)	Specific IgE (class)		
							1	2	3 ⁺
Merrett et al. [32]	Blood donors	7042	57%	NS*	AlaSTAT	6.3	2		4.3
Ownby et al. [33]	Blood donors	1000	53%	38	CAP	3.3	1.4	1.6	0.3
Saxon et al. [34]	Blood donors	1997	56%	NS*	AlaSTAT	5.4–7.6	1.5–3.3	3.5–3.9	0.4–0.5
Senna et al. [35]	Blood donors	1025	84%	39	CAP	3.6	1.7	1.3	0.6
					AlaSTAT	6.4	4.1	1.3	1.0
Garabrant et al. [36]	General population (adult)	5512	NS*	NS*	AlaSTAT	18.6	11.7		6.9
Porri et al. [38]	Attendees for health screening	258	48%	32	RAST	3.5	1.4	1.9	0

*Not stated.

Using a commercial skin test extract, latex sensitization was found in five (0.7%) of 758 Canadian apprentices in baking, animal care and dental hygiene occupations; it was presumed that these had not yet had significant occupational exposure to latex [40]. Using a different test preparation, an identical prevalence was measured among 1175 schoolchildren, of mean age 9 years, in Italy [41]. None of those with positive skin tests in either of these surveys had a clinical reaction to latex.

High-risk populations Several supposedly high-risk populations have been surveyed: in most cases, health-care workers because of their regular contact with latex examination gloves, patients with urogenital abnormalities who have undergone long-term or frequent catheterization or, less often, patients attending allergy clinics. The basis for considering all such populations to be at greater risk than normal is somewhat tenuous and has been questioned [42, 43]; there are, for example, no studies comparing rates of latex sensitization in health-care workers with those in otherwise comparable working populations. Interestingly, no increase in risk of specific latex-IgE production was found among glove-using health-care workers in a large population living in the United States, although there was a small risk among health carers who reported *not* using gloves [36]. However, crude comparisons between health workers and other populations where broadly similar diagnostic criteria have been used, indicate that the former have on the whole a higher rate of positive skin prick tests to latex allergens [44]. Clinical experience appears to bear this out; for example over 60% of cases of latex-associated occupational asthma reported to the UK national surveillance scheme (SWORD – personal communication) has occurred among health-care personnel. Other occupations where glove use is common include catering, food processing and electronics manufacture.

Surveys among health-care staff produce wide disparities in sensitization and allergy rates; the former may differ by as much as 30-fold. These reflect not only variations in phenotype definition and the use of unstandardized immunological techniques and questionnaires but probably also relative exposures to airborne latex allergens although this has been difficult to demonstrate on an individual basis (see below). Unsurprisingly, rates of latex allergy tend to be lower than rates of reported sensitization. A single study has estimated incidence, admittedly in a highly selected subpopulation [45]. Similar variability exists between surveys of patients with spina bifida or related conditions.

Few surveys have been conducted among UK health-care workers. Two had identical methodologies including the use of non-commercial latex extracts for skin prick testing [46, 47]. The remainder [48–50] used a variety of commercial skin test preparations and serum assays but reached similar conclusions. In each case, the very low response rates, both to screening questionnaires and for sensitization testing, make meaningful estimates of prevalence essentially impossible. The surveys do, however, highlight the high frequency of latex-associated clinical symptoms in this occupational group, which cannot easily be attributed to immediate-type latex allergy, occurring in the absence of either a positive skin prick test or immunoassay. The paucity of data relating to UK populations is remarkable and presumably reflects a relatively

low actual or perceived incidence of the disease in this country.

Aetiology

Atopy In all populations, the prevalence of latex sensitization and/or allergy has been associated with atopy, a disposition to produce IgE antibodies to common protein allergens. Estimates of risk may be very high. This is hardly contentious and indeed the absence of such an association would be surprising. Merrett et al. [32] have suggested that latex allergy may arise from an earlier sensitization to grass pollens. This, however, is based on cross-sectional data and must be considered conjectural. Similarly a further reported association, allergic responses to a variety of exotic fruits (see above), is better considered as a co-phenomenon rather than an aetiological 'risk' factor; no consistent temporal pattern for the two has been demonstrated. Among adult populations, a declining prevalence of latex sensitization with age has been reported [32]. This may represent a true age-related effect but equally may arise from a general increase in atopy across time (a 'cohort effect') or an increase in environmental exposure to latex in or before early adulthood (a 'period effect').

Latex exposure The high prevalence of latex sensitization and allergy among health-care workers is attributed to widespread exposure to latex gloves. There are reasonable ecological grounds for this belief; for example, in the United States, the rise in reported cases of latex allergy has closely tracked the increasing import and use of latex surgical gloves to prevent nosocomial cross-infection [51]. Information from other countries is anecdotal only. Detecting exposure-response relationships at an individual level has proved more difficult, and the several cross-sectional analyses that have attempted this have produced conflicting results. Among the explanations for this is the confusion, and probable misclassification, of phenotypic outcomes that will tend to dilute any estimate of the relationship between exposure and response. Liss et al. [52] restricted their study to positive skin prick test responses to a commercial latex extract yet only with difficulty could establish an association with glove use and sensitization among 1350 hospital employees. As with all other studies in this area, however, they examined a cross-sectional population with cross-sectional data on exposure. Each of these may reflect survival pressures; in a US hospital population, for example, nurses with serum positive for anti-latex IgE were more likely to wear vinyl, rather than latex, examination gloves [53].

Exposure studies confirm that levels of airborne latex allergen in hospitals are determined largely by the intensity of glove use [54], and are much higher where powdered surgical gloves are used; indeed, it is difficult to detect any allergen in air when only powder-free gloves are used [16]. It is unclear whether this is attributable solely to the dusting powder or whether there is confounding by high-protein content. Gloves with low-protein content produce less airborne latex allergen [54]. In one (brief) report these observations have been linked to the incidence of latex sensitization or allergy [55]. In a before-after comparison of dental students in Canada, the prevalence of positive skin prick tests was lower following the introduction of powder-free, low-protein gloves into the

dental school [56]; low participation rates, however, preclude the results from being interpreted as anything more than 'suggestive'. The substitution of powdered latex gloves by powder-free alternatives reduced the levels of circulating specific IgE and symptoms in a small group of latex-allergic health-care workers in Germany [57].

Among another high-risk group – patients with congenital urinary dysfunction – the relationships between exposure (in this case, number of surgical procedures) and latex allergy or sensitization appear to be more easily established [58–61]. This is probably because estimates of relevant exposure are less open to error. The relationships appear to be independent of age, sex and atopy. There is little controlled evidence that frequent surgery is a risk factor for latex sensitization in the wider population (see e.g. Bernadini [41]).

Dermatitis Several studies of health-care workers have reported an association between hand eczema attributed to the wearing of latex gloves, and the presence of latex sensitization or allergy. As above, there must be doubts over this apparent relationship but it does raise the intriguing possibility that immediate-type hypersensitivity (including perhaps latex-induced asthma) may in some cases arise from absorption of latex allergens through broken skin.

Diagnosis and management of Type I latex hypersensitivity

Introduction

This section deals with the diagnosis and management of Type I, IgE-associated hypersensitivity to latex. Type IV hypersensitivity (allergic contact dermatitis) from manufactured rubber articles and the more controversial Type IV hypersensitivity to NR latex proteins are discussed elsewhere.

Presentation

Presenting symptoms fall into three main categories: contact urticaria, often on the hands, but which can also be seen anywhere on the body; Type I disease of the upper and lower airways; or anaphylaxis, which may affect previously asymptomatic subjects. In one study, 30% of latex-sensitive children in a high-risk group presented with anaphylaxis [62].

Diagnosis

Diagnosis can be, but is not usually, difficult although a high index of suspicion may be necessary. This is particularly so for anaphylaxis occurring during everyday activities or during surgical procedures in previously asymptomatic patients. Serious reactions have occurred after contact with many common articles, for example after the use of a rubber-handled squash racquet [63]. Although appreciation of high-risk groups is key to the prevention of allergic reactions, a proportion of latex-allergic patients, some of whom have suffered fatal anaphylaxis, do not fall into identified high-risk categories [64, 65]. Severe allergic reactions are especially common after mucous membrane exposure. In animal experiments, latex proteins have been shown to penetrate even intact skin; but are more effective at eliciting an immune

response where the skin is abraded [66]. Atopic or irritant eczema and dermatitis caused by delayed hypersensitivity to rubber chemicals may similarly complicate the clinical picture, particularly on the hands.

History-taking should pay special attention to occupation, the atopic history of the patient, the precise timing of the reaction, with detailing of immediate symptoms, and to the specific circumstances in which it occurred. Special questioning should be directed at previous similar episodes involving eye irritation, sneezing and rhinorrhoea, wheezing, pruritus and/or urticaria after contact with rubber articles, particularly gloves, balloons and much less commonly condoms, or of unexpected symptoms or collapse during dental, medical and/or surgical examinations and procedures. It is relevant to enquire into immediate reactions to fruits. A physical examination should note any eczema, particularly of the hands, urticaria or signs in the upper or lower respiratory tracts. Although even the most careful history will not identify all patients who will subsequently react, there is good evidence that a careful clinical history collected by an experienced physician has a very high sensitivity for clinical latex allergy [67] and is also highly specific, being able for example to distinguish immediate-type reactions to latex from contact dermatitis. There is much less certainty over clinical information collected by questionnaire, the specificity of which is often highly questionable [47]. Currently, there are no standardized and validated questionnaires for use in epidemiological research or health surveillance.

Investigations

Skin prick tests A suspected diagnosis of latex allergy can be confirmed in the majority of cases by skin prick testing and/or commercial immunoassay. There is no current UK marketing authorization for a prick test solution for latex, although several are available from mainland Europe or North America [68, 69]. Solutions of several types of rubber gloves, steeped in saline, are used by some investigators; a minimum of three different known allergenic gloves is recommended [70].

Possibly, the most searching test is tailored to the individual case by pricking through the rubber article thought to have caused the reaction since antigen content varies in different rubber products. [71, 72] Prick testing should be carried out in a relatively 'latex-free' environment and without rubber gloves.

The interpretation of prick test results is made in the light of the patient's history bearing in mind that positive tests can occur in asymptomatic individuals and that the test method may not be wholly sensitive. In the event of a negative prick test response, some investigators proceed to a usage test applying a portion of a glove or a whole glove to the wet hand. This carries a small risk of anaphylaxis [70]. There are no convincing reports of true latex allergy, confirmed by controlled, blinded allergen challenge, occurring in the absence of evidence of specific IgE antibodies.

Immunoassay Commercial immunoassays in common use in the UK are the UniCAP (Pharmacia Ltd, Milton Keynes, UK) and Immulyte/AlaSTAT (Diagnostic Products Corporation, Euro/DPC Ltd, Caernarfon, UK). There are a limited

number of studies, summarized in Table 6, which compare the results of skin prick testing with immunoassay in the same patients. On the whole, the diagnostic performance (particularly specificity) of commercial immunoassays is good in comparison with the results of skin prick testing. Since there are uncertainties about the selection criteria of the subjects included in most of these comparisons, the published estimates are probably optimistic. Several field studies have reported poor agreement between skin prick tests and serological assays [38, 47, 73].

Kim and Safadi [79] reported a relationship between the level of specific IgE and symptoms in patients allergic to latex. High levels were strongly associated with latex-related asthma and urticaria and marginally associated with latex-related rhinoconjunctivitis.

There is more doubt over the meaning which can be attached to a positive IgE test in the absence of clinical symptoms of latex allergy. The presence of latex-specific IgE antibodies detected in the serum of persons with no other evidence of latex sensitization or allergy [80, 81] raises the question of cross-reactivities with other allergens. There is some evidence suggesting that there are common epitopes between latex and other plant products. In a series of Italian blood donors, Senna et al. [35] observed that five out of six individuals with >3.5 kU/L anti-latex antibodies were also sensitized to grass. Similarly, Merret et al. [32], in their series of UK blood donors, were able to demonstrate cross-reactivity between latex and grass pollen in those sera with high levels of IgE anti-latex antibodies. Cross-reactivity has been demonstrated by inhibition experiments between latex, mugwort, ragweed and timothy grass pollen [82], and in one study the specificity of the CAP assay for IgE latex-specific antibodies was found to be highly dependent on the control group, being 100% in non-atopic or dust-mite-sensitive controls but only 60% when mugwort-sensitized controls were used [74]. Cross-reactivity between pollens, fruits and nuts may lead to false positives when determining latex specific IgE and may explain the relatively high prevalence (c. 6%) of latex-specific IgE detected in normal populations.

If both prick test and immunoassay are negative in the face of a characteristic history of immediate hypersensitivity, an alternative diagnosis should be considered. If respiratory symptoms are a feature an inhalation challenge may be considered, but undertaken only in a centre with appropriate expertise. Non-immunological contact urticaria may be

caused by sorbic acid in some glove powders [83]. Casein added to powder during manufacture is reported to have caused immunological contact urticaria in milk-allergic patients [84], and immediate-type reactions may occur from rubber additives [85–88]. Physical urticaria mimicking allergy to latex has also been described [89]. It must be kept in mind that a different allergen may be the culprit or even that the patient has specific IgE antibody to a latex-containing protein absent from the diagnostic materials used.

Management

Patients are advised to avoid contact with latex as far as possible, especially in a health-care setting. Provision of health-care environments which are totally free of latex is rarely possible at present but unnecessary exposure of those known to be sensitive should be scrupulously minimized by appropriate environmental latex screening. A history of clinical reactivity to latex-containing products occurs no more commonly in patients suffering anaphylaxis from latex contact than in those with relatively minor related skin symptoms [90]. It is also clear that some patients are more sensitive than others; if safety is paramount, precautions taken may in some cases prove to have been excessive. At the present levels of knowledge of the disease, with a degree of uncertainty in test interpretation and predictability, it seems prudent that for most patients with clinical and immunological evidence of allergy to latex, avoidance procedures should be strictly observed. In some cases, it is probably sensible similarly to treat patients with suspicions of, but unconfirmed, allergy to latex. Some investigators also treat patients in high-risk categories in 'latex-free' surroundings.

All patients in whom the diagnosis is confirmed should be given detailed written information concerning the nature of the disease and the possible dangers. The information should include details of suitable alternatives to rubber where possible, including non-latex gloves and condoms. Patients should be warned about possible reactions to fruits.

All sufferers should consider wearing a durable bracelet, recognizable as an emergency warning device. Those who have suffered life-threatening reactions after contact with latex should be supplied with, and be taught how, when and where to use adrenaline for self-injection. Alongside the increasing awareness of Type I hypersensitivity there appears to have been an increase in the number of cases seen with

Table 6. Diagnostic performance of serum-specific IgE immunoassays in patients with a positive history of latex allergy and positive skin prick test to latex extract(s)

Author (ref)	Latex allergy	Control	CAP		AlaSTAT		ELISA	
	N	n	S (%)	Sp (%)	S (%)	Sp (%)	S (%)	Sp (%)
Blanco [74]	50	50	86	98	84	98	–	–
		30*	86	60	84	67	–	–
Hamilton [75]	131	181	76	97	73	97	–	–
Kelly [76]	55	50	–	–	–	–	87	66
Ownby [77]	83	60	80	90	75	92	–	–
Carrillo [78]	21	397	76	100	–	–	–	–

*Controls with mugwort allergy. S, Sensitivity; Sp, Specificity.

relatively minor symptoms which have not escalated with time. It would be inappropriate to give such patients adrenaline for self-administration, since there are considerable associated disadvantages for the patient and family concerned. It is not possible at present to identify those in whom symptoms will escalate. It is essential, however, to emphasize to this group the potential for very high exposure to latex in health-care situations. Some investigators supply very sensitive patients with synthetic airway, face-mask and intratracheal tube, as well as a supply of suitable gloves for emergency use. This should become less necessary as knowledge of the disease increases and suitable preventative measures, especially in the emergency services, become the norm.

In all health-care settings, procedures on known latex-sensitive individuals should be carried out in a 'latex-free' environment from which all latex products have been removed or shielded to prevent contact. Patients undergoing surgery should be first on the day's list, and the room, the area to be used and the bed should be clearly labelled. All personnel must wash latex from the hands and face, and change theatre apparel if previous contact has occurred before entering the designated area. Dry rubber products have low levels of extractable protein and extracts do not generally elicit positive prick tests in latex-sensitive patients [91]. There are however, reports of latex molecules in intravenous fluids causing symptoms [92] and probable reactions from release of molecules of latex rubber from the puncture of pharmaceutical closures and giving set ports [93, 94], although one study demonstrated antigen in a phial-stopper only after 40 needle punctures [95]. It is nevertheless sensible to use only drugs stored in glass phials for patients known to be sensitive. It is not known whether this advice should be tempered in cases which are clinically asymptomatic or only mildly symptomatic since some patients appear to remit. Others can suffer increasingly severe reactivity, or present with anaphylaxis as the first manifestation of the disease.

The identification of 'latex-free' equipment is an arduous and very time-consuming task, not made any easier by the lack of mandatory labelling on most items and frequent changes in both manufacturing and supply processes. Although most hospital trusts in the UK have appropriate facilities, the same may not be true for other (smaller) health-care settings including those in primary care, dentistry and the emergency services.

Allergic patients with occupational exposure to latex – commonly health-care workers – need careful advice and support about the avoidance of further exposure. In some cases, this may require a change in occupation, but more often [96, 97] such patients are able to continue work if appropriate changes are made.

Desensitization by graduated exposure of both skin and mucous membranes has been successful in small groups of allergic patients [98–102]. Latex-specific immunotherapy has been reported in a few cases [103]. Neither of these procedures is likely to become widely available in the UK in the near future.

In the UK, there is a patient-support group for those with a diagnosis of latex allergy (Latex Allergy Support Group, PO Box 27, Filey YO14 9YH; web: <http://www.lasg.co.uk>; e-mail: latexallergyfree@hotmail.com).

Type IV reactions to NR latex additives

Allergic contact dermatitis from the various chemicals added to NR latex during its processing has long been recognized [104]. Most such cases are caused by accelerators of vulcanization (thiurams, carbamates and benzothiazoles). These chemicals are all so well established as contact allergens that fresh reports in the literature are now relatively rare, especially those concerning latex gloves, in which the most common Type IV allergens by far are the thiurams [105].

There is not necessarily a distinctive clinical pattern of hand dermatitis in patients with Type IV allergy to latex additives [104]. It is therefore essential to patch test all latex glove wearers who have hand dermatitis with the thiuram mix, mercapto mix (benzothiazoles) and mercaptobenzothiazole (MBT) in the European standard series, and preferably also with zinc diethyldithiocarbamate (ZDC) and zinc dibutyl-dithiocarbamate (ZBC). The widespread use of thiurams in latex makes it important to be aware of less obvious sources in thiuram-sensitive patients, such as cosmetic sponge applicators [106]. Thiurams are also used as agricultural and horticultural fungicides.

Dermatitic reactions to glove powder (cornstarch) are usually due to adsorbed thiurams, though protein contact dermatitis from cornstarch has been described [107]. Rarely, the face can be the sole site of thiuram allergy in a glove wearer [108]. Much rarer sources of Type IV allergy in latex gloves include the antimicrobial cetyl pyridinium chloride [109]. Type IV allergy to latex itself has been described [110], though this has been disputed by some [111].

There is no evidence that atopics are inherently any more (or less) susceptible to Type IV allergy to latex additives. While there is also no firm evidence of any immunological association between Type I latex allergy and Type IV latex additive allergy, the fact that the compromised skin of the dermatitis caused by Type IV latex additive allergy may be more easily penetrated by Type I latex allergens may make the two occur together more often than by chance [112].

Patients with allergic contact dermatitis from latex additives require advice as to appropriate synthetic rubber or plastic (e.g. vinyl, polyurethane) alternatives, especially gloves [104, 105].

Latex allergy in urology

Risk factors

The high prevalence of latex sensitization and allergy among children with spina bifida probably reflects their high exposure to surgery and/or indwelling medical devices. Ellsworth et al. found an overall prevalence of latex allergy of 60% in 50 spina bifida children, with a significantly higher frequency of previous urological surgery in those with allergy. There was no difference, between those who had latex allergy and those who did not, in age, the number of years that they had been using intermittent, clean self-catheterization or the number of abdominal operations that they had undergone [59].

However, there are probably other factors to consider. The presence of latex-specific IgE was found in 25% of a group of

European spina bifida patients aged 2–40 years. Multivariate analysis showed that atopy, fruit allergies, and a history of five or more operations were significantly and independently associated with latex sensitization [113]. On the other hand, in a controlled study of the prevalence of latex allergy as defined by a skin prick test and *in vivo* diagnostic kit, it was found that 26% of spina bifida patients had symptomless latex allergy compared to 5% of patients from an ear, nose and throat clinic even though both groups had had the same mean number of operations. There were no positive skin prick tests in a control group of urological patients who had had no operations [114]. Latex allergy has also been found in 1% of patients on regular haemodialysis [115].

Presentation

About a third of American spina bifida patients will have a history of allergic reactions to latex products [59]. The level of awareness of the problem amongst spina bifida children and their families in the UK has been low and so the symptoms should be specifically sought. In some cases, the association is obvious, but in others it may be obscure, such as itchy eyes while using washing-up gloves. In occasional patients, there is acute anaphylaxis under anaesthetic.

During medical procedures on spina bifida patients, latex use should be reduced to a minimum; in some cases, it has been abandoned altogether. There are important warning signs that may alert the clinician to the problem in a previously unsuspected case. In a group of five allergic children who were undergoing transurethral bladder stimulation and urodynamics, all had coughing or sneezing for several minutes before bronchospasm and generalized allergic reactions developed [116].

Management

The most important part of management is identification of patients at risk and prophylaxis. As the prevalence is high in spina bifida patients, a specific enquiry should be made for symptoms in all patients. Minor reactions can be treated with bronchodilators, antihistamines and, occasionally, steroids. It should be remembered that minor reactions may be the forerunner of major anaphylaxis.

All who have a suggestive history or unexplained hypotensive episodes under anaesthetic should undergo skin testing and measurement of latex specific IgE. A latex-free medical environment should be created for patients found to be at risk. All operating theatres should have a written protocol that includes lists of latex-free equipment.

Applications to anaesthesia and treatment of anaphylaxis

Background

As sensitization to latex is becoming more widespread [117] there is increasing pressure on all health-care institutions to develop protocols to identify and deal with individuals allergic to latex in a latex-safe environment. Because of the ubiquity of latex in health-care settings the risk of allergic reactions is high and the prevention of exposure to the allergen is essential in order to avoid adverse outcomes.

During surgery, the most severe forms of Type I hypersensitivity, respiratory failure and anaphylactic shock, generally occur in the perioperative period when mucosal, parenteral and inhalational exposure to latex protein is most likely. Anaesthetists play a central role in the care of the majority of patients during this period of high risk of serious allergic reactions. They are therefore in a favourable position to help develop and implement latex allergy protocols and to educate hospital staff. Furthermore, they will also invariably have to provide crisis management in case of any generalized allergic reaction in awake and anaesthetized patients.

Strategies for creating a latex-safe hospital environment have been published including lists of latex-free alternatives for commonly used items [118–121]. It should be pointed out that in dealing with latex allergy, human error is probably the most important factor, and raising staff awareness and vigilance is of crucial importance.

Frequency and presentation

The incidence of anaphylactic reactions associated with anaesthesia is estimated to range from 1:5000 to 1:25000 anaesthetics with a mortality of 3.4% [122]. The onset of latex anaphylaxis can, unlike the frequently immediate reaction in drug-induced anaphylaxis, occur with a delay of several hours [123]. It might therefore be difficult to establish a temporal relationship with allergen exposure, and latex must be considered as a possible cause in every case of suspected anaphylaxis. A French multi-centre database identified latex as the trigger of perioperative anaphylaxis in 0.5% of all cases in 1989, rising to 12.5% in 1991, 19% in 1994 and 16.6% in 1996 [124, 125].

The most frequent initial symptoms of anaphylaxis during anaesthesia are hypotension, increased airway pressure and a generalized erythema [125, 126]. Other clinical signs include urticaria, angio-oedema (swelling) of the face and larynx, coughing and wheezing and tachycardia.

Management

Preoperative pharmacological prophylaxis with antihistamines and corticosteroids in patients with latex allergy is currently not generally recommended because of lack of scientific data proving the efficacy of this strategy in IgE-mediated reactions [121]. There are several case reports demonstrating the failure of pharmacological prophylaxis to protect against severe allergic reactions [123, 126]. In addition, this approach is also thought to mask early symptoms of latex allergy and create a false sense of security, potentially leading to greater exposure.

Untreated anaphylaxis is rarely survived and appropriate therapy must be started promptly. The Association of Anaesthetists of Great Britain and Ireland in cooperation with the British Society of Allergy and Clinical Immunology has published guidelines for the management of adult patients with suspected perioperative anaphylaxis [125]. These guidelines apply regardless of the cause of anaphylaxis, and are divided into initial and secondary therapy. Similar treatment recommendations have been published by the American Society of Anesthesiologists [118]. Certain subgroups of patients at high risk of latex allergy consist mainly of

children. The Resuscitation Council of the United Kingdom has recently published consensus guidelines for the treatment of anaphylactic reactions in children [127]. The treatment algorithm needs to be modified for children under anaesthesia, but the general principles of treatment are identical to those in adults.

Clinical practitioners may need to be flexible in the application of these guidelines according to the individual circumstances and their personal experience. If the patient is undergoing a procedure at the time of the allergic reaction, the procedure should be terminated as soon as possible. Because it can initially be difficult to exclude latex as a potential trigger we recommend that all items known or suspected to contain latex be removed from the patient in every case of anaphylaxis. The Association of Anaesthetists of Great Britain and Ireland also recommends regular 'anaphylaxis drills' including all members of staff that would be involved in case of a real emergency.

After initial stabilization, every patient with a systemic allergic reaction needs to be monitored closely by experienced staff in a high dependency or intensive-care area where comprehensive cardiovascular and respiratory monitoring is readily available. There must be a complete report in the case notes, and the patient and the general practitioner must be fully informed. The event may usefully be reported to the Adverse Incident Centre at the Medical Devices Agency (Hannibal House, London SE1 6TQ).

Dentistry

Dental health-care Workers

The number of dental personnel affected by latex allergy is unknown but all are at risk because of regular use of latex gloves. Most studies have been cross-sectional, some conducted by questionnaire [128], others using skin prick tests [129, 130]. Hamann et al. [129] investigated the prevalence of Type I reactions to latex by performing skin prick tests with eluates prepared from latex gloves; 6.2% of dental personnel tested positive. Tarlo's study of Canadian dental students suggested an increasing incidence of positive skin prick tests with progression through the dental course (0% years 1 and 2, 10% year 4) [130]. There are no data on the prevalence of latex allergy among UK dental personnel.

Dentists have been advised to use powder-free, NRL gloves because of the risk of creating latex aeroallergens, which pose a potential risk to both dental personnel and patients [120]. Latex gloves with low levels of allergens and extractable latex proteins are also recommended.

The dental management of patients with latex allergy

Dental practitioners must be aware of individuals who are at high risk of developing Type I hypersensitivity reactions to NRL; careful history taking is a prerequisite. It has been suggested, for example, that non-latex gloves should be used for all spina bifida patients undergoing dental treatment.

The creation of a 'latex-free' environment in the dental surgery is difficult, since many items of dental equipment contain latex [120]. There is no current databank listing

dental devices that contain latex, and manufacturers have to be contacted on an individual basis to obtain specific information. Three main items of equipment which contain NRL are in routine dental use: latex gloves worn by staff, dental rubber dams and local anaesthetic cartridges. Other potential sources that may come into contact with the patient include: rubber, (prophy) cups, rubber stoppers on endodontic files and devices used as handgrips on instruments. Affordable, non-latex examination and procedure gloves are made from synthetic materials, such as nitrile. Vinyl and other plastic gloves are not suitable since they do not offer the flexibility of latex and are generally more permeable to blood and water than latex gloves [131]. Sterile gloves made from synthetic rubbers are available for surgical procedures, but are expensive.

Dental rubber dams are fitted to provide a moisture-free environment during root canal therapy and the placement of restorative materials. They also protect the patient's airway from the inhalation of small dental instruments or materials. Rubber dams contain significant levels of latex proteins [132], and have been reported as causing Type I reactions in latex-sensitized individuals [133]. Dental dams manufactured from synthetic materials are now available. Some local anaesthetic cartridges, for use in dentistry, may have bungs or seals manufactured from latex, and these are best avoided in patients with confirmed allergy. It is essential to check with the manufacturers concerning current manufacturing processes of dental cartridges, as these can change [134]. Cross-reactivity between gutta percha (used to obturate root canals) and latex has been anecdotally reported in a health-care worker [135], but appears to be extremely rare. Alternative materials such as titanium or acrylic points may be used.

It is important that all dental practices institute a management protocol for latex-sensitized patients and that staff are aware of the issues involved. Non-latex delivery of emergency drugs and resuscitatory measures must be available to deal with medical emergencies in dental practice. Dental health-care workers should also be encouraged to report any adverse reactions they suffer, when in contact with latex gloves, and to seek specialist advice and appropriate testing.

Occupational health issues and practice

Reporting, legislation and guidance

In the UK, there is a statutory requirement to report cases of occupational asthma and urticaria to the Health and Safety Executive [136]. These conditions are also prescribed under the industrial injuries disablement benefit scheme and workers may apply for compensation [137]. It is however probable that cases recorded by these schemes considerably underestimate the true incidence of these conditions.

UK health and safety law does not explicitly address latex; however, protection of exposed workers from latex allergy is implicit in several pieces of health and safety legislation. The Health and Safety at Work Act 1974 expects employers to ensure the health, safety and welfare of their employees, as far as is reasonably practicable. The Control of Substances Hazardous to Health (COSHH) regulations 1988 and the

Management of Health, Safety and Welfare regulations 1992 expect a hierarchy of protective measures to be instituted, and where a risk still exists, regular health surveillance of exposed workers. In the National Health Service, regular health surveillance would be very time consuming because of the large number of exposed workers. Most employers take a pragmatic approach, educating staff about the health effects and encouraging them to report symptoms of possible allergy to their occupational health department.

There is national guidance for health care organizations from the Medical Devices Agency (MDA) of the Department of Health. In 1996, the MDA advised UK health-care establishments to implement medical glove policies for staff [138] and in 1998 issued a safety notice reinforcing this with specific reference to powdered gloves: 'local policies (should) address the circumstances under which powdered gloves may be used and provide a justification for their continued use, especially in areas of high usage or increased risk such as operating theatres' [139]. Similar guidance was published by the Department of Health in 1999 [140].

On the basis of the evidence for the role of powder in initiation of lung sensitization, and the Medical Devices Agency advice, it may now be considered indefensible for health-care establishments to continue routinely to supply powdered latex gloves to staff. In addition, employees need ready access to non-latex gloves should they develop an allergy to latex. Ideally, all staff should have access to latex substitutes.

Primary prevention

Arguably, enough is known about the broad aetiology of latex allergy for preventive action to be taken. A small number of successful examples have been published. At an ecological level, a joint programme of education and regulation in German hospitals was followed by a remarkable change in glove purchase patterns and, 2 years later, by a reduction in reported cases of latex asthma [141].

More specifically, there is weak evidence that primary preventive programmes are successful in reducing the incidence of latex sensitization in children with congenital urinary tract abnormalities. Small-scale, before-after comparisons in Spain [142] and Germany [143] suggest reductions in units that operate a latex-free clinical environment.

Summary

1. The apparent increase in Type I latex allergy probably reflects a true increase in incidence, beginning in the late 1980s. The cause(s) of this remain unexplained but plausible explanations include the increasing use of latex goods in several settings.
2. Although the condition is probably rare in the general community, it may be much commoner among certain high-risk groups: in particular those with congenital urinary dysfunction and those who wear (powdered) latex gloves of high-protein content at work. There is a paucity of evidence, but latex allergy appears to be less common in the UK than in otherwise similar countries.

3. NR latex contains a large number of allergenic proteins. These may be of differing importance depending on the route of exposure.
4. A diagnosis of immediate-type latex allergy should only be made in the presence of a clear and characteristic history together with immunological evidence of specific IgE production from either skin prick testing (preferable) or immunoassay.
5. The diagnostic accuracy of both skin testing and immunoassay remain a matter for further study.
6. Skin prick testing and immunoassay should be conducted only by persons experienced both in the techniques and in their interpretation. Skin prick testing should be avoided in patients with a history of latex anaphylaxis.
7. Patients with a diagnosis of Type I latex allergy should have the condition carefully explained to them and be advised to follow appropriate avoidance measures. During all health-care procedures they should be treated in a 'latex-free' environment.
8. In the majority of cases where there is workplace exposure to latex, allergic patients can be managed without a change in occupation.
9. A high index of suspicion should be maintained by all those caring for persons at high risk of developing latex allergy; this applies particularly to those who undergo regular, invasive treatment(s) such as patients with congenital urinary dysfunction.
10. There is sufficient knowledge of the broad aetiology of latex allergy for primary preventive programmes to be widely adopted.

Recommendations

1. The unnecessary, 'routine' use of latex gloves should be identified and discouraged through appropriate risk assessment. Where their use is necessary, only powder-free gloves of low extractable protein content should be used. This should apply not only to all health-care settings but also to other places of work where glove use is common.
2. An unambiguous system of labelling for all health-care equipment would greatly ease the task of identifying suitable latex-free items for the care of sensitized patients. Manufacturers should be encouraged to develop such a system rapidly.
3. Further work on the production of (licensed) diagnostic tests of high sensitivity and specificity is required.
4. Systematic surveillance and intervention studies should be continued and/or initiated in order to identify the most (cost-) effective means of preventing Type I latex allergies.

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