

Latex Allergy: An Emerging Operating Room Problem

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Anaphylactic reactions under anesthesia occur in 1:5,000 to 1:25,000 anesthetics, with a 3.4% mortality (1). Anaphylactic reactions to intravenously administered drugs may occur in approximately 1:5,000 to 1:15,000 anesthetic inductions (2). Recently, anaphylaxis to latex products has been reported both outside of and inside the operating room. Latex-based medical products are ubiquitous in the health care environment. Surgeons, operating room nurses, and anesthesiologists handle latex products daily, rely upon their routine use more than ever since the adoption of universal precautions, and constantly expose themselves and patients to these products. This article will review the rapidly proliferating current literature on latex allergy, its particular incidence in certain pediatric patients, and the success of several strategies for the prevention and treatment of latex anaphylaxis.

Evaluation of IgE Sensitivity in Latex Allergy

Several assays are useful in the evaluation of IgE-mediated latex anaphylaxis. The skin-prick test (SPT) is accomplished by dropping antigen in solution (1:10 wt/vol) onto glabrous skin and pricking the skin gently with a needle through the solution while observing for 10 min for a wheal and flare reaction. The incidence of untoward reactions is small, but this method is less sensitive than intradermal testing (IDT). For IDT, the solution is injected intradermally in a dilution from 100- to 1000-fold less than the SPT, and the reaction is usually graded subjectively as 1+ to 4+. IDT carries a larger risk of systemic reaction, however, because the antigen cannot be wiped from the skin (3). Newer assays include the basophil histamine release test (BHRT) and lymphocyte proliferation tests (LPT), examined in 15 patients with latex contact urticaria. The BHRT was positive in 13/14 (93%), in comparison to commercial radioallergosorbent testing (RAST) positivity in 9/15

(60%). Cell-mediated immunity may be an additional factor, because the LPT was positive in 3/15 (20%) (4).

The RAST is an *in vitro* test for IgE antibodies to a specific allergen, accomplished by exposing solid-phase allergen to antibody-containing serum. This complex is incubated, reexposing the solid-phase allergen-antibody complex to radiolabeled anti-IgE antibody, and bound radioactivity is measured. The activity is proportional to the quantity of IgE antibody bound during the initial phase of the test. It is not yet a substitute for the previously described SPT and IDT. RAST concordance with SPT may vary from 59% to 93%, depending on the allergy being tested. False negative determinations may occur in 10–16% of cases, and false positives in 11–15%. RAST testing for latex allergy is improving. Jaeger et al. (5) found a correlation of 82% between IgE RAST and latex SPT, but direct skin testing remains more sensitive, less time-consuming, and less expensive than RAST (3), albeit carrying a risk of allergic reaction. The latex allergosorbent test (LAST) is another alternative, which avoids radioisotopes, can be performed in less than 6 h, and correlates with an *r* value of 0.92 to the latex RAST (6).

Consultation should be obtained with an allergist during the preoperative evaluation of the latex-allergic patient. Following an acute reaction, consideration should be given to delaying testing, as the latex-specific IgE titer may actually decrease following the reaction, and the acutely treated patient may have residual effects from sympathomimetics, antihistamines, or steroids.

Clinical Reports of Latex Allergy and Intraoperative Anaphylaxis

Contact dermatitis to rubber products has been recognized for many years; most of the agents invoked in the past were part of the rubber manufacturing process itself and not latex. The vulcanization of rubber enhances its elasticity through the cross-linking of polymer chains and is accomplished by slow heating in the presence of sulfur. Additional chemicals are added for strength, stretch, and durability, such as accelerators in the curing process (mercaptobenzothiazole, thiurams,

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Table 1. Latex Allergy and Pediatric Patients

Author (Reference)	No. patients	No. episodes anaphylaxis	Primary diagnosis
Axelsson et al. (19)	3	3	Atopy
Gerber et al. (18)	2	4	Bladder exstrophy
			Esophageal atresia
Slater (20)	2	2	Myelodysplasia
Moneret-Vautrin et al. (21)	3	3	Myelodysplasia
Swartz et al. (22)	1	1	Myelodysplasia
Calenda et al. (23)	1	2	Inguinal hernia
Kelly et al. (24)	11	12	10/11 Myelodysplasia
			1/11 GU tract abnormality
Gold et al. (25)	15	19	Myelodysplasia or
			GU tract abnormalities
Gaignon et al. (26)	1	1	GU tract abnormalities
Nguyen et al. (27)	10	6	Myelodysplasia or
			GU tract abnormalities
Merguerian et al. (51)	1	2	Myelodysplasia
Holzman et al. (48)	29	29	28/29 Myelodysplasia
			1/29 GU tract abnormality

GU = genitourinary.

and dithiocarbamates) and antioxidants (phenylenediamine and others) (7). Contact urticaria to rubber was reported by Nutter in 1979 (8) and was confirmed by skin-prick testing as IgE-mediated in 1984 (9). Contact urticaria to latex surgical gloves (in three operating room nurses) was also found to be IgE-mediated (10). Immediate hypersensitivity characterized by flushing, tachycardia, urticaria, angioedema, a choking sensation, wheezing, and abdominal cramping was reported in an operating room nurse just after she had gloved for surgery (7). She had a 4+ reaction to skin prick, and demonstrated 17.7% binding (control 4%) to latex-specific RAST. RAST testing, as well as SPT, was used to confirm the IgE mediation of reactions to rubber by Axelsson et al. in 1987 (11). RAST testing may be less sensitive than SPT, however; Turjanmaa et al. (12) found that in hospital workers who were latex allergic, skin-prick testing and whole glove use testing correlated well, but half of the allergic patients had negative RASTs. This study concluded that RAST testing may not be as sensitive as SPT for mildly allergic patients. Anaphylaxis due to mucosal exposure was reported by Sondheimer et al. in an 18-yr-old woman with a previous history of contact urticaria to latex who underwent the insertion and inflation of a balloon fashioned from a latex glove to perform rectal manometry (13). Ownby et al. reported anaphylaxis associated with latex allergy during barium enema examinations in six patients, with one death (14). Two additional patients experienced contact urticaria and anaphylaxis with oral and vaginal exposure to condoms and rectal exposure to a latex glove (15). In October 1990, a manufacturer of latex balloon enema tips voluntarily recalled all latex-containing products when it became clear that of 148 incidents related to barium enema ex-

aminations reported during a 22-mo period, nine fatalities occurred, and of the nine, three were anaphylactic in nature *before the instillation of barium* (16,17).

Severe intraoperative anaphylaxis in children was reported by Gerber et al. (18). One patient had repeated intraoperative episodes of anaphylaxis before latex was determined to be the etiology; another patient was suspected of having latex allergy after the first episode and subsequently tested positive. Both patients had undergone numerous surgical procedures. Three cases of anaphylaxis and angioedema resulting from blowing up balloons were reported in children with significant atopic histories by Axelsson et al. in 1988 (19). Two of the three children avoided rubber balloons for several years and developed negative RAST tests. Presumably the IgE-specific concentration decreased with time in the absence of allergen exposure. Clinical articles in the US and Canada followed in rapid succession (Table 1) (20-27).

A variety of popular (lay and medical) press warnings about latex allergy have appeared. In February 1990, the *AMA News* warned physicians to "watch for latex reactions" in their patients (28). In May 1991, the monthly newsletter of the American Society of Anesthesiologists reiterated an FDA Medical Alert with regard to allergic reactions to latex-containing medical devices, a notice which was formalized in the July 1991 bulletin (29,30). The *Morbidity and Mortality Weekly Report* cited the FDA recommendation that all patients be screened for potential latex allergy, particularly those with myelodysplasia, and that once latex allergy is suspected, use of nonlatex items should be considered. The Public Health Service further recommended considering postponement of elective surgical procedures for these patients.

Occupational Health Risks for Operating Room Personnel

Health care workers and hospital employees may be at risk for progressive sensitization to latex (31). Turjanmaa surveyed 512 hospital employees and found 7.4% of doctors and 5.6% of nurses allergic to latex (32). The overall hospital employee frequency was 3%; 67% of these 15 latex-allergic employees had a history of atopy. In fact, rubber glove use on eczematous hands may predispose to the development of latex allergy. Charpin et al. found a 10.6% incidence of natural latex skin test positivity among 248 operating room nurses; 41% reported skin "itchiness" when wearing gloves (33). Wrangsjö et al. evaluated 30 patients with a contact urticaria history to gloves, contraceptives, balloons, or dental dams, and found 13 who belonged to medical occupations, and 25/30 who had a history of atopy (34). Twenty-one of thirty had elevated IgE values, and 25/30 were RAST-positive to pure liquid latex extract. SPT was found to be the most sensitive diagnostic tool (30/30), while RAST testing was positive in 25/30. Low total IgE values were related to false negative RAST testing. Fuchs and Wahl studied 31 latex-allergic patients; 71% worked in the medical field (35). Finally, Moneret-Vautrin et al. (36) studied 907 physicians, surgeons, nurses, and hospital employees and found 18/907 with a history suggestive of latex allergy. SPT was positive in 18/18 (100% sensitivity), with 883/889 SPT negative (99% specificity). They also studied eight children with spina bifida without a history of latex allergy and found 4/8 positive to latex SPT and RAST.

Mechanisms of Anaphylaxis in Latex Allergy

Direct IgE mediation appears to be the pathogenesis of the anaphylactic response to latex. Exposure to a foreign substance can lead to IgE-mediated anaphylaxis when a susceptible person comes in contact with an allergenic protein in its native state or as a hapten. The IgE antibody then becomes attached to high-affinity receptors on mast cells and basophils. During reexposure, the antigen causes degranulation of the cells through cross-linking, inducing a membrane change leading to calcium ion influx, alterations in cyclic nucleotide levels, and the release of preformed and rapidly produced mediators of anaphylaxis. This subject has been well reviewed (37-39).

At least four polypeptides from natural latex have the ability to bind specific human IgE. These proteins have approximate molecular masses of 10, 24, 35, and 100 kDa (40). Confirming an earlier hypothesis by Meding and Fregerts (41), these were found to be soluble proteins.

Slater (42) succeeded in separating five bands of proteins by electrophoresis in 14 of 24 children with spina bifida who were seropositive to latex and found that the 14-kDa band developed seropositivity in 14/14 patients. Other bands indicated a reduced amount of seropositivity (20 kDa band, 6/14; 23 kDa band, 5/14; 27-28 kDa band, 2/14; 41 kDa band, 0/14), suggesting that the 14-kDa peptide is a major antigen in latex allergy. Alenius et al. (43) determined that the 14-70-kDa protein band was allergenic, with the 14- and 21-kDa bands showing the most intense reactions in natural rubber, whereas 11- and 26-kDa bands were only seen in glove extract. IgG₄ antibodies also have been found recently in sera of latex-allergic patients (44). Allergenic proteins of similar molecular mass have been found by others as well (40, 45).

Slater et al. found a 34% incidence of seropositivity by RAST to latex in unselected myelodysplasia children (46). Within the myelodysplasia group, those who were positive had a history of a rubber-associated allergic episode (intraoperative or otherwise) 45% of the time. One patient of 21 found to be antibody negative also gave a positive clinical history as well. Meeropol et al. have surveyed parents of spina bifida patients in five myelodysplasia clinics in the New England Myelodysplasia Association (a sample of 187 families) and found an incidence of allergy to catheters, gloves, balloons, or more than one item in 18-28% (47). Parents reported symptoms ranging from rashes and contact urticaria to watery eyes, wheezing, and respiratory arrest.

Our experience at Children's Hospital, Boston, has evolved during the last 5 yr with 36 patients who manifested signs and symptoms of latex anaphylaxis in the operating room during surgical procedures (48). Thirty-four of 36 patients had myelodysplasia; one patient had Rokitsky syndrome (agenesis of the vagina) and another had exstrophy of the bladder. Physiologic findings during the intraoperative events are illustrated in Figure 1. Approximately 150-180 patients per year with myelodysplasia come to our operating room for surgical procedures.

Thirteen patients with latex allergy, all of whom have experienced an allergic or anaphylactic episode previously, have returned to the operating room for 28 surgical procedures. None of these patients were prepared with H₁/H₂ receptor antagonists or steroids, and latex exposure was scrupulously avoided pre-, intra-, and postoperatively. There were no recurrences of anaphylaxis. In one instance where cardiac catheterization was performed, the balloon catheter was washed thoroughly with freely flowing sterile saline before insertion, and no signs of allergy were noted.

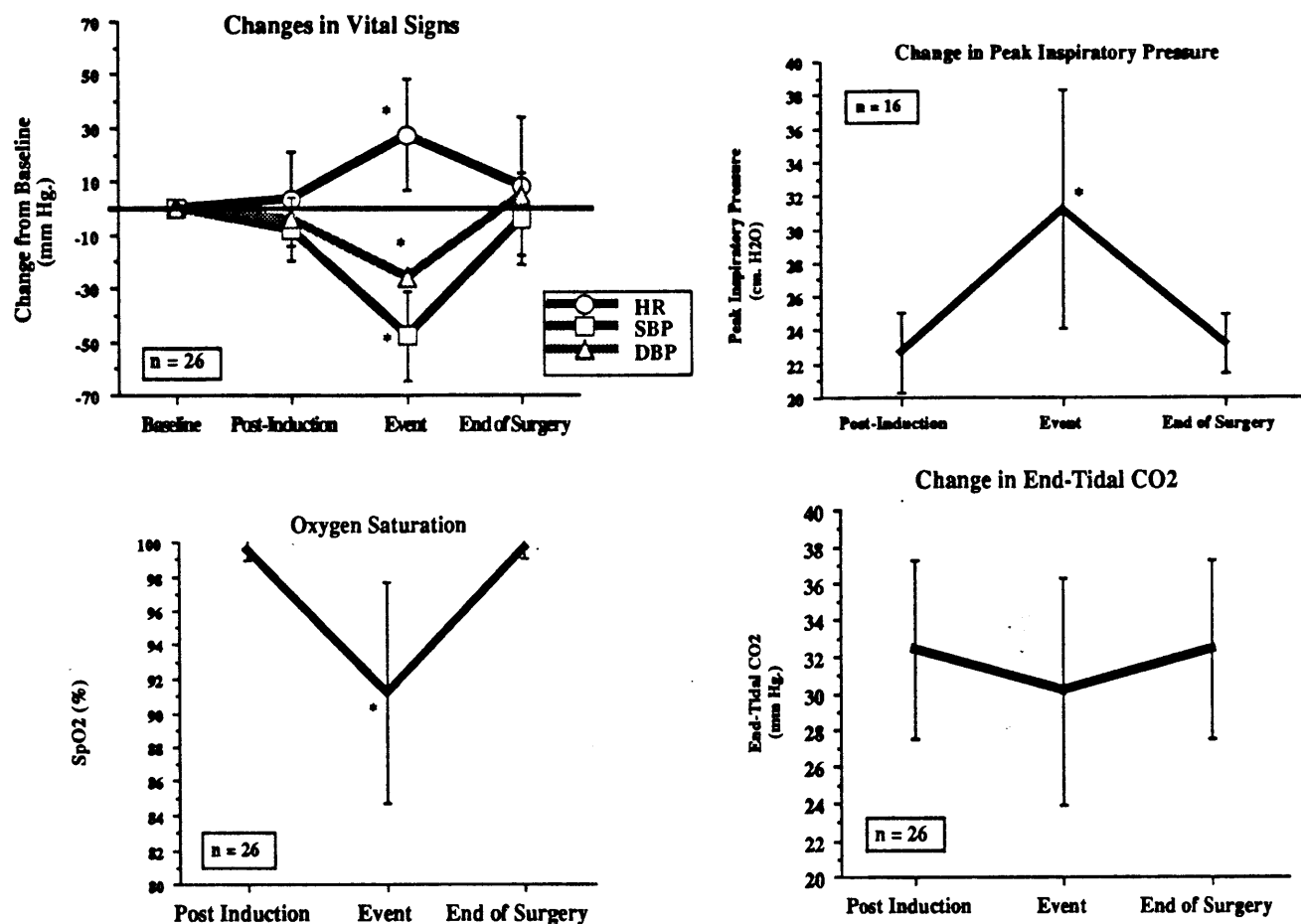


Figure 1. Experience with intraoperative latex anaphylaxis, Children's Hospital, Boston, 1987-1991. HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure. * Significant at $P < 0.05$.

Specific Recommendations

Preventive measures are key to the successful and safe management of patients with latex allergy. A careful history in suspect individuals, particularly those with multiple allergies, atopy and/or eczema, and occupational contact with latex-based products is crucial. The available data suggest that up to 50% of patients with myelodysplasia may be allergic to latex, and the majority will have historical evidence for this allergy. Other patients requiring intermittent self-catheterization such as spinal cord injury, complex urological, and chronic care patients should be evaluated thoroughly with latex allergy in mind. Patients who return to surgery for multiple procedures (genitourinary reconstructive procedures, repeat dilations for esophageal strictures) should be included in this group as well. Specific answers to a past history of balloon or household glove intolerance, and allergic symptoms at the dentist, should be sought.

When available, allergy testing may provide documentation as well as reassurance for patients. Preoperative testing, however, is not uniformly recommend-

ed; Slater and Mostello (49) have recommended against routine testing for latex allergy in myelodysplasia, whereas Moneret-Vautrin et al. (36) support prospective testing of myelodysplasia patients.

The role of pharmacologic prophylaxis, short-term desensitization, or immunotherapy as an adjunct to the care of these patients likewise is not well established. Sockin and Young reported the successful return to the operating room of a 36-yr-old woman who experienced intraoperative anaphylaxis during a cesarean section, and who subsequently was evaluated as latex allergic (50). She underwent resection of a colon carcinoma. Operating room equipment containing latex was replaced with non-latex substitutes, and the patient was treated with a preoperative regimen of diphenhydramine, cimetidine, and methylprednisolone, without anaphylactic symptoms. Another case report detailed the successful return to the operating room twice subsequently to intraoperative latex anaphylaxis in a patient who was also prepared with hydrocortisone, diphenhydramine, and ranitidine (36). Although a urinary

Table 2. Checklist for Latex-Allergic Patients

<i>Preoperative</i>	
	Patients with a history of chronic care with latex-based products, e.g., spina bifida patients
	History of intolerance to latex-based products: balloons, rubber gloves, condoms, dental dams, rubber urethral catheters
	History of intraoperative anaphylaxis of uncertain etiology
	Careful coordination of surgical/anesthesia/nursing teams
	Check with central supply for availability of alternatives
<i>Intraoperative</i>	
Anesthesia equipment	
Gloves	
Airways/endotracheal tubes	
Masks	
Rebreathing bags	
Ventilator bellows	
Circuit	
Multidose vials	
Intravenous equipment/tourniquets/rubber bands	
Blood pressure cuffs	
Syringe plungers	
Surgical equipment	
Drains (e.g., penrose)	
Urinary catheters	
Instrument mats	
Surgical gloves	
Rubber-shod clamps	
Vascular tags	
Bulb syringes for irrigation	
Rubber bands	
<i>Postoperative</i>	
Medic alert tag	
Warnings posted on chart	
Warnings posted on bed	

catheter was not utilized during the two follow-up procedures, latex surgical gloves were, and other latex products were not specifically avoided. Finally, Mercurian's patient underwent her surgical procedure following two prior anaphylactic episodes after being prepared with H₁ and H₂ receptor antagonists (diphenhydramine and cimetidine) and prednisone (51). Latex was strictly avoided during her care. Nevertheless, although pharmacologic prophylaxis is cited in these case reports, it is not as effective as avoiding the allergen. Our experience with 13 latex-allergic patients returning to the operating room for 28 surgical procedures suggests that an effective latex-free environment can be established. A checklist may be helpful as a reminder (Table 2), but a vigilant attitude is more important.

Avoidance of contact with or manipulation through latex devices is of paramount importance. Alternative, non-latex surgical gloves are critically important. Turjanmaa et al. went on to test the allergenic properties of 19 brands of

latex gloves and found that not all brands possessed the same antigenicity (52). Furthermore, the amount of total protein eluted from a specific brand did not predict the degree of allergenicity. Glove ingredients were evaluated further by Belozzer and Storrs (53). Leynadier et al. have reported successful suppression of allergenicity in natural latex surgical gloves by revising the manufacturing process through initially washing and then exposing the gloves to saturated steam sterilization at 120°C centigrade for 1 h; protein content became undetectable in four of five glove supernatants (54). They further found it possible to evaluate allergenicity through changes in electrical conductivity. Powdered gloves have been shown to produce symptoms due to aerosolized latex antigen (5), and may contribute to occupational asthma (55,56). Neoprene (Neolon®, Deseret Medical Inc., Sandy, UT) or styrene-butadiene block polymer (Elastyren®, Hermal Pharmaceutical Laboratories, Inc., Oak Hill, NY) should be substituted for latex-containing gloves, whether powdered or unpowdered, because all latex-containing gloves have varying amounts of allergen (10). Clinicians should be aware, however, that these gloves are not as comfortable to work with as latex gloves; they are relatively inelastic, more difficult to put on and take off, and do not "breathe" as well, therefore contributing to hand heat and moisture retention during the period worn.

Instrumentation of latex injection ports on intravenous bags or tubing must be avoided. The use of syringe/stopcock methods or unidirectional valves for injecting medications is advocated. Multiple-dose vials with natural rubber stoppers should not be instrumented (57). The top of the vial may be removed, or another preparation of the same medication in ampule form may be used. We have not had any problems with freshly drawn and administered drugs in rubber-tipped plunger syringe systems even in patients who are latex allergic, but glass syringes may be a more acceptable alternative. Although it is unlikely that the application of a rubber-based blood pressure cuff to the skin of the upper arm will result in anything more than a contact dermatitis, this problem is easy to avoid by wrapping the area under the cuff with soft cotton and placing the cuff over the wrap. Alternative cuff materials may be available. The surgery, nursing, and anesthesia team must work closely together and communicate before bringing the patient into the operating room, so that everyone is thinking about avoiding exposure to latex, rather than trying to rigidly fit a program for the patient according to a "protocol." We use several prominent signs in the operating room to serve as constant reminders, because we are all so habituated to routine care with latex-based materials.

Concurrent factors that increase the severity of anaphylactic reactions or interfere with successful treatment include treatment with β -blocking agents or the presence of asthma. The use of epinephrine in patients treated with β -blockers may lead to unopposed α -adrenergic effects, and result in severe hypertension.

Other disease entities that may mimic anaphylaxis should be considered. Loss of consciousness may result from vasovagal syncope, seizures, myocardial infarction, and arrhythmias. Acute respiratory failure may occur during status asthmaticus, epiglottitis, presence of a foreign body, and pulmonary embolism. Similar cutaneous manifestations may occur with mastocytosis, carcinoid, hereditary angioedema, and skin manifestations of drug reactions.

Pharmacologic support for anaphylaxis should be readily available for known or suspect individuals. We prepare epinephrine in concentrations of 100 $\mu\text{g}/\text{cc}$ and 10 $\mu\text{g}/\text{cc}$, and administer 0.1 $\mu\text{g}/\text{kg}$ (e.g., 7 μg , or 0.007 mg in a 70-kg patient) for signs and symptoms of anaphylaxis. Doses of epinephrine recommended for resuscitation during cardiac arrest are *not* the same as those required for the treatment of anaphylaxis and may lead to severe supraventricular tachycardia or ventricular dysrhythmias including ventricular tachycardia requiring resuscitation. We occasionally have needed to administer isoproterenol in addition to epinephrine to clear severe bronchospasm. Aerosolized bronchodilators should be readily available as well.

Coordination with the Post Anesthesia Care Unit and floor nurses should be carried out so that the patient care area is clearly marked and all personnel are familiar with the patient's intolerance for latex products. A Medic-Alert® tag should be arranged for during the hospitalization and worn by the patient thereafter because these patients will often return to emergency rooms for treatment.

Conclusions

Intraoperative anaphylaxis is not commonly encountered in the practice of anesthesiology. An increasing population of children and young adults who are veterans of surgical interventions, as well as the adoption during the past few years of universal precautions and routine wearing of latex gloves, has increased the awareness of latex allergy. Experience at Children's Hospital, Boston, and many other institutions suggests that this is a relatively common problem in children with multiple exposures to latex products, such as those with myelodysplasia. Furthermore, evolving experience seems to suggest that health care professionals should be aware of the manifestations and treatment of latex allergy for their own sakes as an occupational hazard. Finally, manufacturers should be sought who will

contribute actively to improved labeling and product alternatives for the safety of all concerned (58).

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