

New perspectives on propofol allergy

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Purpose. Propofol is an intravenous sedative used in many patient populations and care settings. Although generally considered safe and effective, the drug has historically been avoided in patients with reported allergies to egg, soy, and/or peanut on the basis of the manufacturer's prescribing information. Concerns exist for potential adverse events, increased medication costs, reduced efficacy, and risk of medication errors when using alternative agents. Here we present a critical examination of the literature concerning cross-reactivity of food allergies with propofol to provide evidence-based recommendations for the evaluation and management of potential allergic reactions.

Summary. Literature regarding the history of propofol allergy warnings and clinical trial data were assessed to provide an alternative perspective on avoidance of propofol in patients with food allergies. Suspected trigger molecules are discussed with evaluation of the antigenic potential of excipient ingredients used in the manufacture of multiple propofol formulations. Evidence-based recommendations are provided for pharmacist-led screening of adult patients with reported food allergies to support selection of propofol or alternative therapy.

Conclusion. There is a lack of definitive evidence that propofol must be routinely avoided in patients with reported allergies to egg, soy, and/or peanut products. Data from clinical trials suggest that propofol is safe for patients with nonanaphylactic food allergies. Patients who do experience allergic reactions following administration of propofol should undergo further testing to definitively identify the specific trigger and prevent future unnecessary avoidance

of preferred medication regimens. Pharmacists can play an important role in interviewing patients with reported food allergies to better determine the risk vs benefit of propofol avoidance.

Keywords: allergy interview, anaphylaxis, food hypersensitivity, propofol

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Propofol is an intravenous anesthetic widely used to provide moderate and deep sedation for numerous medical and surgical indications across all patient populations and in many care settings. Although generally considered safe and effective for most patients, the drug is associated with severe and potentially life-threatening reactions, including type 1 immunoglobulin E (IgE)–mediated anaphylactic immune responses.¹⁻³ Published case reports often link apparent anaphylactic reactions to a reported patient history of egg or soy allergy as the etiology. The correlation between these specific food allergies and risk of anaphylactic reaction to the lipid emulsion used as a vehicle for propofol administration is detailed in the manufacturer’s prescribing information and pharmacy literature.⁴⁻⁶ However, propofol is often administered concurrently with other medications, and detailed information about patients’ prior allergic reactions, the timing and results of their most recent skin prick testing, and other information required to definitively associate these reported reactions with propofol is not usually available.

Emerging evidence challenges the assumption that patients with certain reported food allergies have an increased risk of an allergic reaction to propofol, and there is legitimate clinical equipoise regarding the risk vs benefit of administering propofol to patients with reported food allergies or withholding one of the most effective and well-studied anesthetic medications available. Unnecessary avoidance of propofol could potentially lead to increased use of other medications with higher cost, lower efficacy, or increased risk of adverse events and medication errors.⁷

We conducted a search of the PubMed, Google Scholar, and MEDLINE databases to identify primary literature, using the following search terms in various combinations: propofol, allergy, food allergy, anaphylaxis, egg allergy, and soy allergy. The reference

sections of identified primary literature articles were also scanned for additional citations. The available literature describing use of propofol in patients with food allergies is reviewed here with the intention of exploring the complexities of diagnosis and alternative potential triggers for apparent anaphylactic reactions to propofol. Keeping in mind the lack of definitive evidence that avoidance of propofol in patients with reported food allergies is of critical importance, we examine the history of propofol, food allergies, screening techniques, and alternative propofol formulations to offer evidence-based management strategies for mitigation of potential allergic reactions in at-risk patients.

Propofol allergy and anaphylaxis

One estimate of the incidence of propofol anaphylaxis is 1 in 60,000 exposures.⁸ Propofol has been definitively identified as responsible for approximately 1% to 2% of anaphylactic reactions during anesthesia events, but techniques for pinpointing a specific allergic trigger are complex, time sensitive, and not usually the priority of clinicians.⁹ Definitive diagnosis and reporting of propofol allergic reactions are not typically prioritized above immediate patient care, and the reaction is often superficially blamed on the simplest and most recognizable potential culprit: food allergy. Thus, the underlying etiologic trigger of an apparent anaphylactic reaction to propofol may not be clear, and false identification of allergic etiology has implications for future patient care (Table 1).

Initial propofol formulations dating back to the 1970s included cremophor, a castor oil-based substance, as the emulsifying agent. Because of a high incidence of anaphylaxis, the product was reformulated in 1986 as a soy oil (100 mg/mL) and egg yolk lecithin (12

mg/mL) emulsion.¹⁰ Case reports of anaphylaxis continued with the new formulation, and the product labeling was revised in the United States and Australia to list egg, soy, or peanut (based on concern for cross-sensitivity to soy) allergy as a contraindication to use; however, nationally approved prescribing information may vary by country or manufacturer.^{6,11-13}

Egg, soy, and peanut allergies are thought to be most strongly tied to the foods' protein component, with these proteins occasionally contaminating purified oils used in pharmaceutical manufacturing.^{10,14} Derived from egg yolk, the purified egg lecithin phosphatide found in propofol emulsion contains such miniscule amounts of residual egg protein that it is unlikely to trigger an immune response. Pharmaceutical-grade soybean oil is similarly unlikely to contain notable quantities of soy protein and is so highly refined that residual proteins present in the product are significantly modified or denatured.⁸ When potentially allergenic food proteins are present owing to contamination, the amount of protein can be variable or only present in certain lots of the medication.^{14,15} Although the propofol product does not contain peanut oils, an incidence of cross-reactivity between primary peanut allergy and allergies to other legumes has been demonstrated.¹⁶

A growing incidence of food allergies worldwide is perhaps driving increased concern regarding the use of propofol in this population.¹⁷ Recent survey data estimate that 19% of the US population self-reports some kind of food allergy, although only about half of these individuals can describe symptoms consistent with clinical evidence of allergic reaction.¹⁸ Specifically, egg allergy is estimated to clinically affect 2 million US adults and soy allergy affects 1.5 million US adults, collectively representing fewer than 1% of Americans. Incidence of true food allergy in young children is thought to be significantly higher, with up to 2.5% of children reporting egg allergy.¹⁹ Thus, food allergy-based contraindication to

propofol may have a larger impact on children than on adult populations. Notably, most individuals outgrow childhood egg allergies by adulthood, so egg allergies documented in the medical record may not be fully accurate.²⁰

Survey data and retrospective medical record reviews suggest that prescribers often avoid use of propofol in patients who report egg, soy, or peanut allergies. Martínez and colleagues²¹ surveyed 26 allergy departments affiliated with medical centers in Spain to determine whether they habitually avoid propofol exposure in patients with reported allergy to egg. Although only 2 facilities had a formal protocol or policy in place, the large majority of responding institutions and practitioners (77%) continue to recommend avoidance of propofol in these patients. Mehta and colleagues²² reviewed medical records for 1,365 esophagogastroduodenoscopies, including 15 procedures on 12 pediatric patients with a history of egg anaphylaxis. The investigators found that propofol was used significantly less often in patients with reported egg allergy (72% of cases without allergy vs 40% of cases with documented allergy, $P < 0.0001$). However, they found no difference in rates of anesthesia complications, as not a single anaphylactic event was reported during any of the procedures. Together, these data suggest that propofol can be safely used in populations with egg allergies even though this is commonly avoided by prescribers.

Several other retrospective studies have challenged the contraindication listed in propofol prescribing information through reports of safe use of propofol in patients with documented allergies to egg-, soy-, or peanut-containing foods. Molina-Infante and colleagues²³ reported a series of 404 endoscopies performed under propofol sedation in 60 adult patients with reported egg, soy, and/or peanut allergies, all of whom had a positive skin prick test or serum IgE test confirming the food allergy; no instances of propofol

reaction were identified in this review. Murphy et al¹ identified 28 pediatric patients with a history of IgE-mediated clinical reaction to egg who received at least 1 administration of propofol. Of the 43 propofol exposures, only 1 instance of propofol use (2% of cases) resulted in an immediate nonanaphylactic allergic reaction, which occurred 15 minutes after propofol administration in a patient with multiple food allergies and a history of anaphylactic reaction to egg.

Furthermore, Asserhøj and colleagues²⁴ found no evidence of a link between egg, soy, or peanut food allergies and propofol reaction in a 2-part retrospective study. First, 153 adult patients with a suspected allergic reaction to propofol were evaluated, 4 of whom were eventually diagnosed with confirmed propofol allergy on the basis of positive skin prick tests and repeat-exposure challenges. None of the 4 patients had allergic symptoms when eating egg, soy, or peanut, and none had detectable levels of egg- or soy-specific IgE in serum. Next, the investigators reviewed 171 anesthetic charts from 99 adult patients positive for IgE specific to egg, soy, or peanut and an exposure to propofol and found no instances of allergic reaction. Sommerfield and colleagues²⁵ conducted a similar review in which they identified 304 children with allergies to egg, peanut, soybean, legumes, or a combination of the 4 (reported allergy rates of 66%, 74%, 9%, and 4%, respectively), finding no difference in rates of allergic reaction to propofol in this group when compared to nonallergic children exposed to propofol. These authors collectively conclude that propofol allergy is not reliably predicted by documented food allergy and suggest that propofol is probably safe for most patients with reported food allergies.

Additional potential triggers of allergic reaction to propofol include the preservatives disodium edetate (EDTA) and metabisulfite, which are present in various formulations of the

product and have been known to cause allergic or bronchospastic reactions in other individuals (Table 1).²⁶ More specifically, the branded product Diprivan (Fresenius Kabi, Lake Zurich, IL) contains EDTA, while generic versions are more likely to contain sulfites, which are a particular concern if used in asthmatic patients.^{8,27} Because the branded and generic versions of propofol can be made with different excipient or preservative ingredients, it can be difficult for providers to distinguish between formulations and to compare allergy risks across them (Table 2).

Some authors have suggested that patients may be allergic to functional group components of the propofol molecule rather than to excipient ingredients. Laxenaire et al³⁰ support this theory by presenting a case series of 14 patients (ages 12-70 years) with apparent allergic reactions to propofol brought in for follow-up skin and serum tests 4 to 6 weeks after the incident. None of the 14 patients studied had any known exposure to propofol or lipid emulsions before their clinical reaction, although 9 individuals described in the series had prior allergic reactions to other medications, including antibiotics, lidocaine, or neuromuscular blocking agents. Of these 14 patients, 13 had some positive response to propofol (Diprivan) during follow-up skin prick tests. Four of these 13 patients had a positive skin prick test for propofol but a negative skin prick test for the lipid emulsion vehicle. Two patients were positive for skin prick test reactions to both propofol and neuromuscular blocking agents. These authors suggest that preexisting IgE may have had specific binding sites for the phenyl nucleus or isopropyl groups on propofol, both of which are common to many other medications, including neuromuscular blocking agents. Ultimately, these researchers were unable to identify a strong, predictable association of allergic reaction between propofol and lipid emulsion vehicle.

Figure 1 shows the molecular structures of the active and excipient ingredients in propofol formulations commonly implicated as suspected triggers of apparent allergic reaction. As shown in the figure, propofol has a high degree of hydrophobic character conferred by an aromatic ring and 2 isopropyl groups. Gangineni et al³¹ have suggested that propofol's diisopropyl groups serve as epitopes for antibody binding in an immune-mediated allergic response. Additionally, Laxenaire et al³⁰ have suggested the phenyl ring in propofol as a possible causative source of allergic response. However, marked hydrophobic characteristics, including phenyl rings, isopropyl groups, and other long-chain carbon structures, occur in numerous therapeutics that possess very low antigenicity. Some examples of these therapeutics are shown in Figure 1, namely, lidocaine, rocuronium, carisoprodol, and warfarin. While it is known that propofol is more hydrophobic than any of the 4 other therapeutics shown, carisoprodol contains an isopropyl group and a propyl group, lidocaine contains a propylamine group and a phenyl nucleus, warfarin contains a phenyl nucleus, and rocuronium contains a large number of cyclobenzyl moieties and other hydrophobic characteristics. Additionally, some of the excipients in common propofol formulations (EDTA, linoleic acid, lecithin, and phosphatidylethanolamine) have also drawn scrutiny as possible causative agents in allergic response. Again, these molecules share many of the structural features of propofol, including hydrophobic carbon character, branched and unbranched carbon chains, and conjugation. However, the small study by Laxenaire et al³⁰ showed that the lipid emulsion carrier system, which contains linoleic acid and phosphatidylethanolamine, had no correlation with allergic response in patients who had an apparent allergic event while receiving propofol.

As described above, published literature has implicated structural features of propofol or common excipients in propofol formulations as suspected triggers of potential allergic reactions. In our opinion, the vast differences in the chemical structures of molecules implicated in cross-reactivity to propofol shown in Figure 1 complicate prediction of propofol allergy on the basis of a patient's history of food or drug allergy. The phenyl nucleus or isopropyl groups on the propofol structure can also be found on similar molecules with very low antigenicity, and avoidance of propofol is not widely recommended for patients with documented allergies to similar compounds (including antibiotics, lidocaine, or neuromuscular blocking agents).

We conclude that there is no "one-size-fits-all" rationale for apparent allergic reactions to propofol administration. Patients may develop allergic responses to food antigen contaminants, excipient ingredients, or molecular structures and functional groups common to other therapeutic agents. Data suggest poor correlation between an observed reaction to propofol and prior reactions to other possible triggers. Thus, avoidance of propofol based strictly on patient report of food allergy is not a rational practice founded in strong clinical evidence, and providers should equally consider prior allergic reactions to other medications when evaluating propofol allergy risk. Truly, the most reliable predictor of allergic reaction to propofol seems to be prior reaction to propofol or the lipid emulsion vehicle.

Alternative formulations

The desirable characteristics of propofol (quick onset, short duration, potential for deep sedation, etc) as compared to other available anesthetics strengthen the need for additional formulations that maintain these desirable traits while further minimizing the risk of allergic reaction. While the current lipid-based emulsion formulation of propofol has significantly fewer reports of allergic reaction than the original cremophor solvent formulation, concerns about continued allergic reactions and the risk of infection associated with lipid formulations have led researchers to seek alternative preparations.¹⁰

These investigations led to the development of fospropofol disodium, a water-soluble phosphate ester prodrug of propofol, which is formulated as an aqueous solution.³² The aqueous solution allows for removal of the soybean oil and egg lecithin carriers previously described as potentially responsible for allergic reactions. While the prodrug formulation may have delayed onset owing to its inherent nature, studies have shown no difference in overall clinical effectiveness.³² While this formulation avoids the risk of allergic reaction to food components in the lipid emulsion, patients may still react to the drug molecule or other excipient ingredients in the formulation (Table 2). At this time, there is little additional information on the pharmacoeconomics or pharmacokinetics of fospropofol in comparison to propofol infusion, and the drug is currently in limited use worldwide, for procedural indications only.²⁸

A 2% propofol formulation recently gained emergency use authorization from the Food and Drug Administration (FDA) as a result of drug shortages experienced during the coronavirus disease 2019 (COVID-19) pandemic.²⁹ This product contains 20 mg/mL propofol as compared to the 10 mg/mL traditional formulation, yet the products contain an equal

amount of lipids (0.1 g/mL). Thus, the more concentrated 2% formulation reduces the overall lipid content received by the patient but does not remove the potential for vehicle-based adverse events. Similarly to the generic 1% formulation, the 2% formulation does not utilize EDTA as a preservative (Table 2).

Recommendations for screening and drug selection

In spite of the recommendation found in the manufacturer's prescribing information, propofol has been safely administered to hundreds of patients with a reported egg allergy. Thus, most experts conclude that propofol use is likely to be safe for the majority of egg-allergic patients who do not have a history of egg-related anaphylaxis.^{1,15,33} Continued recommendations to avoid propofol in egg anaphylaxis may be justified primarily by the medical tradition of *primum non nocere*, in an abundance of caution when considering the potentially fatal implications of anaphylactic reactions.¹⁵ On the basis of the findings in the study by Laxenaire et al,³⁰ prior allergic reaction to neuromuscular blockers may also be a predictor of propofol reaction worth consideration and additional study.

The infrequency of propofol anaphylaxis contributes to the difficulty in identifying enough patients to generate a strong scientific evidence base on which to make clinical practice recommendations; however, some expert consensus groups have offered guidance.^{9,21} Indeed, the American Academy of Allergy, Asthma, and Immunology endorses the use of propofol in patients with histories of soy and egg allergies, stating that, while patients can experience allergy to propofol, it is not typically tied to either of these substances.³³

A surge in the need for allergy testing in the setting of antimicrobial stewardship has created additional opportunities for pharmacists as healthcare providers. Several states have passed statutes allowing pharmacists to perform skin testing on patients with penicillin allergies to reduce the inappropriate use of broad-spectrum antibiotics.^{34,35} Because egg allergy is one of the most frequently reported food allergies, it could be beneficial for pharmacists to participate in the preoperative patient care setting to confirm or rule out potential allergies to anesthetics such as propofol. Traditional methods of skin prick testing for “egg allergy” would not be useful in predicting propofol allergy, as the egg lecithin in propofol is a yolk component and egg allergy skin testing evaluates reactions to egg albumin proteins found in egg whites.³⁶ The most direct way of evaluating a propofol allergy is with a skin prick and/or intradermal test using propofol as the injected antigen. Initially, the skin prick test is performed by administering 1 mL undiluted propofol percutaneously. Next, a more sensitive intradermal test is performed using a 1:1,000 dilution of propofol administered intracutaneously.³⁷ If pharmacists sought to extrapolate the positive outcomes seen by programs implementing penicillin skin testing, specific training programs required for penicillin testing could be adapted to include information on dosage preparation, injection technique, and results interpretation specific to propofol testing.

Because resources and expertise for skin prick testing are not always widely available, increased use of allergy interviews has been proposed as a means of removing labels for patients with allergies that unnecessarily impede medical care. Pharmacists could potentially play a significant role in distinguishing which patients with reported egg allergies might in fact be good candidates for propofol use by conducting “allergy history” interviews. In Table 3, we adapt a common structure for a “drug allergy interview” to include a series of

screening questions specific to propofol and food hypersensitivity.^{38,39} When documenting the results of such allergy interviews in the medical record, food and medication allergies should be documented separately. As much information as possible about the date, features, and objective evidence of a prior reaction should be included to inform future patient care decision-making.⁴¹

Following a thorough allergy screening, pharmacists may recommend 1 of 4 strategies: (1) proceed with propofol administration, (2) perform a propofol skin test, (3) administer a trial dose of propofol, or (4) administer premedications to reduce the likelihood of an allergic reaction. Figure 2 depicts an approach that may be utilized in determining the most appropriate next step in management of this patient subset.

Administration of propofol without further testing is appropriate for the majority of patients. All patients with nonanaphylactic reactions to egg may receive propofol safely based on the results of previous studies. Although virtually no evidence guides the recommendation that propofol be avoided in patients with anaphylaxis to egg, some providers may feel more comfortable administering propofol following a propofol skin prick test (described above), administration of a trial dose, or administration of premedications.^{15,21}

Some experts recommend consideration of a small trial dose of propofol in patients with a history of egg anaphylaxis.^{21,37} Also known as a drug provocation test (DPT), the purpose is to administer enough of the drug to elicit an immune response, but not enough to cause a severe reaction. The recommended provocation dose is one-tenth of the full bolus dose, which is considered the gold standard for allergy confirmation.⁴² If the DPT is well tolerated, the full anesthetic dose could then be used.

Premedication with corticosteroids and/or histamine antagonists is another strategy that may be employed in this population. Prednisone 1 mg/kg (maximum of 50 mg) or the equivalent plus diphenhydramine 50 mg intramuscularly or orally with or without a histamine H₂-receptor blocker (famotidine 20 mg or equivalent) given before the procedure has been suggested to reduce the severity of allergic reactions in at-risk patients.⁴³ However, evidence for this practice is lacking, and concerns about delayed hypersensitivity reactions cloud the utility of this option.⁴⁰

Management of anaphylaxis

All medical personnel should be appropriately trained to recognize and treat anaphylaxis, as an urgent response is critical to positive patient outcomes. Anytime propofol is administered to patients with a history of egg allergy, all care providers should be made aware of the increased potential for anaphylaxis in the specific patient case. Clinical features of anaphylaxis are severe, long lasting, and potentially misleading. The most common signs appear within minutes of intravenous administration of propofol and include cardiovascular (hypotension, tachycardia, or loss of pulse) and cutaneous (facial flushing, hives, and rash) symptoms; however, cutaneous reactions can be difficult to identify because of sterile draping or hospital gowns.^{9,21}

If a patient develops signs or symptoms of anaphylaxis during anesthesia, administration of all agents likely to have caused the anaphylaxis should be immediately discontinued. Providers should call for assistance, including additional support and supervisory personnel. Emphasize airway control, provide 100% oxygen, and prepare for

rapid intubation, which frequently becomes necessary. Administer parenteral doses of epinephrine and fluids for circulatory support, antihistamines, systemic corticosteroids, and inhaled bronchodilators according to current management guidelines.^{9,44}

Postreaction follow-up

Guidelines from the Association of Anesthetists of Great Britain and Ireland lament the difficulty medication safety experts face in determining the true incidence of adverse reactions to anesthetic medications such as propofol due to low rates of event reporting by clinicians.⁴⁴ Additionally, these experts describe the importance of further investigation and postreaction follow-up to determine whether the observed reaction was truly anaphylactic in nature. Rising levels of serum mast cell tryptase, a protein contained within mast cells, can be monitored in the 24 hours after the reaction to assist in determination of the type of reaction, and appropriate blood samples for laboratory testing should be drawn as soon as possible after the reaction. Following the patient's recovery, an experienced allergist can assist with intradermal testing and interpretation of test results to limit the influence of false-positive or false-negative results.³³ This analysis is vital in isolating the offending agent from what is often a group of potentially allergenic co-administered medications.

All apparent allergic reactions should be documented in the patient's medical record, and as much information as possible should be included about the incident to inform future decisions about potential medication exposure risk. Additionally, the reaction should be documented in the national medication safety monitoring repository (FDA's

MedWatch in the United States, available at

<https://www.accessdata.fda.gov/scripts/medwatch/index.cfm>).

Conclusion

Despite a formal contraindication in the manufacturer's prescribing information, there is a lack of definitive evidence that propofol should be routinely avoided in patients with reported food allergies to egg, soy, or peanut products. Evidence from clinical trials suggests that propofol administration is safe for patients with nonanaphylactic food allergies. Pharmacists can play an important role in interviewing patients with reported food allergies to better determine the risk vs benefit of propofol avoidance. Alternative formulations, provocation doses, skin testing, and premedication are additional options for patients at the highest risk or with a history of allergic reaction to propofol.

Disclosures

The authors have declared no potential conflicts of interest.

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Figure 1. Structures of propofol, common excipients in propofol formulations, and common therapeutics that have structural features similar to those of propofol. Shown are the chemical structures of therapeutic and excipient ingredients of propofol formulations that have been studied either as a causative agent or as a predictor for propofol allergy. The structures share some common chemical characteristics, namely, appreciable hydrophobicity and ionization at physiological pH (aliphatic amines and organic acids). Conversely, the structures are quite diverse in their molecular weights, binding potentials, LogP and cLogP values, and 3-dimensional confirmations (higher LogP or cLogP indicates greater hydrophobicity). From a purely chemical standpoint, there is nothing notable that is common among the majority of structures for molecules that are known to elicit an allergic response. In fact, there are many therapeutic agents with virtually no allergenic profile that share the most common features, including appreciable hydrophobicity and ionization at physiological pH (for example, warfarin).

Figure 2. Suggested pharmacist approach to risk stratification for egg allergy and recommendation for propofol use. The diagram depicts suggestions for how a pharmacist might approach risk stratification of each type of reported allergic reaction and subsequent recommendations for propofol administration or avoidance. GI indicates gastrointestinal.

Key Points

- There is a lack of definitive evidence that propofol must be routinely avoided in patients with reported food allergies to egg, soy, or peanut products.
- Propofol may be used safely in patients with nonanaphylactic reactions to foods used in the manufacture of pharmaceutical excipients, namely egg, soy, and peanut.
- Pharmacists can recommend and/or conduct allergy screening and interviews to identify patients with reported food allergies who can safely receive propofol.

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Table 1. Possible Triggers of Apparent Anaphylactic Reactions to Propofol

Antigen (Ingredient Type)	Patient Population at Risk	Brand or Manufacturer	Potentially Safer Alternative or Formulation
Egg protein contaminants (excipient)	Egg-allergic patients	All brand and generic formulations of propofol	Fospropofol ^a
Soy protein contaminants (excipient)	Soy-allergic patients	All brand and generic formulations of propofol	Fospropofol ^a
Soy protein contaminant cross-sensitivity (excipient)	Peanut-allergic patients	All brand and generic formulations of propofol	Fospropofol ^a
EDTA (preservative)	EDTA-allergic patients	Diprivan ⁶	Generic formulations containing sulfite-based preservatives, 1% propofol, 2% propofol, or fospropofol ^a
Metabisulfite (preservative)	Sulfite-allergic, asthmatic patients	Some generic formulations	Diprivan
Cross-allergy to functional groups within the molecule	Unknown, other comorbid drug allergies	All brand and generic formulations of propofol	Alternative anesthetic agent

Abbreviation: EDTA, disodium edetate.

^aFospropofol was approved by the Food and Drug Administration in December of 2008 but has since been discontinued by the manufacturer.

Table 2. Comparison of Excipient Ingredients in Various Propofol Formulations

Manufacturer	Product	Common Excipients	Excipient Differences
Fresenius ⁶	Diprivan	Propofol, soybean oil, egg lecithin, sodium hydroxide	EDTA, glycerol
	Propofol 1% generic	Propofol, soybean oil, egg lecithin, sodium hydroxide	MCT, glycerol, oleic acid
	Propofol 2% ²⁹	Propofol, soybean oil, egg lecithin, sodium hydroxide	MCT, oleic acid
Pfizer	Propofol 1%	Propofol, soybean oil, egg lecithin, sodium hydroxide	Glycerol, sodium benzoate, benzyl alcohol
Actavis ¹²	Propofol 1%	Propofol, soybean oil, egg lecithin, sodium hydroxide	Glycerol, sodium benzoate
Sagent ¹³	Propofol 1%	Propofol, soybean oil, egg lecithin, sodium hydroxide	Glycerol, sodium metabisulfite
Dr. Reddy's	Propofol 1%	Propofol, soybean oil, egg lecithin, sodium hydroxide	Glycerol, benzyl alcohol
Eisai ²⁸	Fospropofol ^a	Fospropofol ^a , monothioglycerol, tromethamine	None

Abbreviations: EDTA, disodium edetate; MCT, medium-chain triglycerides.

^aFospropofol was approved by the Food and Drug Administration in December of 2008 but has since been discontinued by the manufacturer.

Table 3. Proposed Screening Questions for Evaluating Egg Allergies in Patients Expected to Receive Propofol

Screening Question ^{38,39}	Rationale
What happens if you eat eggs? Is the effect different when scrambled, hard boiled, or baked?	Various protein epitopes responsible for egg allergies result in differing reaction types. Some epitopes are deactivated during cooking and subsequent digestion processes, resulting in the majority of individuals being able to tolerate consumption of cooked eggs, particularly when boiled or baked. ¹⁹
Are you able to tolerate egg whites or yolks separately?	The primary epitopes implicated in egg allergy are found in egg whites. Allergy to egg yolk is rare and typically seen in adults with bird-egg syndrome. ¹⁹
What happens if you touch eggs or birds?	Egg livetins are small water-soluble proteins found in egg yolk and are implicated in individuals with contact allergies to eggs or birds (bird-egg syndrome). This manifests as respiratory symptoms when exposed to birds or allergic symptoms when egg is consumed. ¹⁹
Have you ever received anesthesia? When?	Prior anesthesia history may indicate whether the patient has tolerated propofol previously. Furthermore, allergic reactions that occurred in childhood are often alleviated with age. ¹⁹
What other allergies and conditions do you have?	Reactions to other medications or excipient ingredients such as lipid emulsion, metabisulfite, and disodium edetate may indicate a potential reaction to propofol. Certain conditions such as asthma are linked to higher-severity food allergies. ⁴⁰

Figure 1. Structures of propofol, common excipients in propofol formulations and common therapeutics that share structural features similar to propofol.

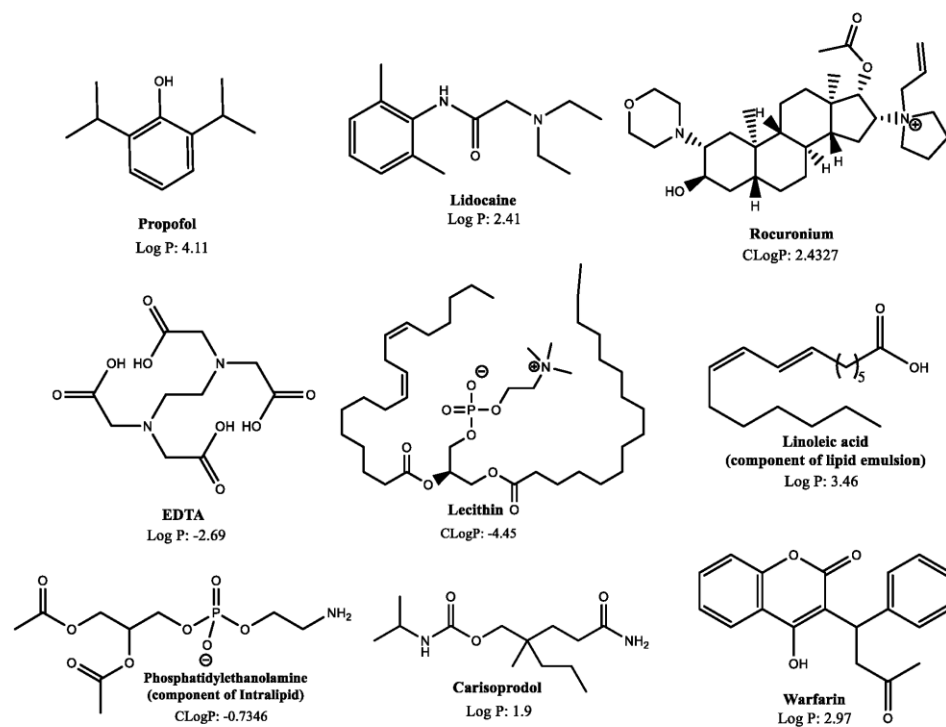
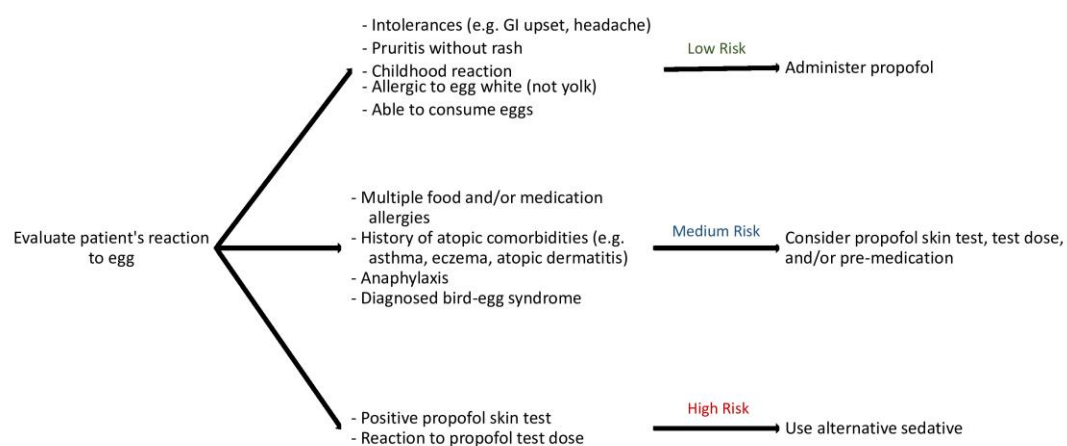


Figure 2. Suggested Pharmacist Approach to Risk Stratification for Egg Allergy and Recommendation for Propofol Use



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