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Coring of Intravitreal Medication Vial Stoppers: A Report From the Research and Safety in Therapeutics Committee of the American Society of Retina Specialists

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Abstract

In 2024, the American Society of Retina Specialists (ASRS) Research and Safety in Therapeutics (ReST) Committee became aware of reports of coring of vial stoppers in relation to preparation of intravitreal injections. A literature review was performed to further understand and characterize this occurrence within the context of retina practice and the broader medical community. Relevant articles were identified through a systematic search of PubMed using predefined criteria. Coring can be observed when a needle punctures the rubber stopper of a medication vial, pushing a small piece or pieces of the stopper material into the container and introducing extrinsic particles into the drug product. Factors associated with coring include larger gauge needles, perpendicular needle entry, multiple-use vials, and thicker rubber stoppers. Rubber stopper thickness and composition also influence the likelihood of coring. To prevent patient safety issues from coring, filter needles are commonly used to draw up medications from vials because they are effective in mitigating particulate matter from entering syringes. No documented cases of clinical complications related to coring in ophthalmology have been identified. Coring represents an unreported phenomenon in the preparation of intraocular medications. Although there have been no safety implications in retina practice related to coring and intravitreal drug vials, these reports underscore the importance of careful medication preparation, inspection of vials, the use of appropriate needles, and adherence to best clinical practices.

Keywords

coring, intravitreal injection, medication preparation, safety

Introduction

The term "coring" refers to the process by which small pieces of a medication vial's stopper material (usually rubber) are sheared off by the needle during insertion.[1] This can introduce foreign particulate matter into the syringe-vial system, potentially depositing it into the vial of medication, remaining within the needle, or staying in the syringe used to draw up the medication. PubMed was used to search for the terms "coring" and "vial" to further understand and characterize this phenomenon.

The vial stopper material, vial size and type, needle or cannula size and type, and angle of needle puncture may influence the likelihood of coring.[2] The true incidence of coring is unknown; however, a wide incidence range, from 3.1% to 40% in the medical literature, has been reported.[3–5] Iatrogenic complications related to coring have been reported, including occlusion of venous access devices, pulmonary infarction and granulomas, neurologic sequelae from paradoxic embolism, anaphylaxis in patients with latex hypersensitivity, and death.[3]

In contemporary retina practice, coring is most relevant in the context of medication preparation for intravitreal (IVT) injections, but may also occur in the clinic and operating room

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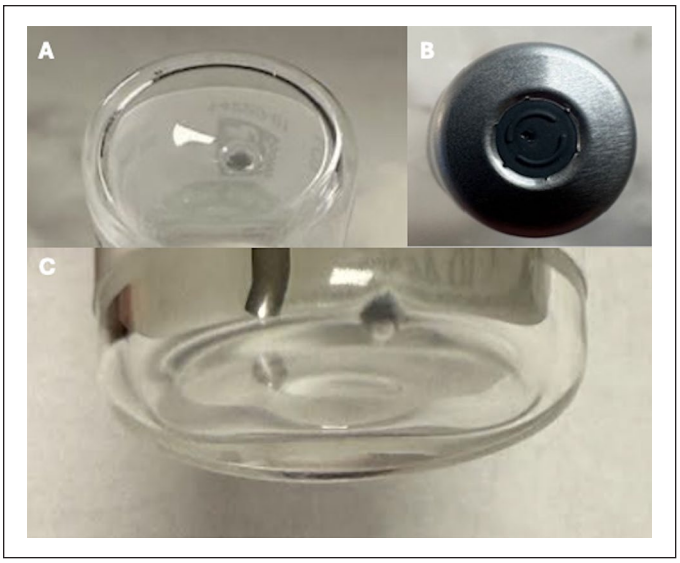

Figure 1. (A) Coring material at the base of intravitreal (IVT) drug vial #1 with surrounding imprint in the glass from the needle's impact. (B) Coring of the rubber stopper. (C) Coring material at the base of IVT vial #2.

while preparing anesthetic or perioperative medications. Notably, any vial of medication that is to be used for intraocular injection may be susceptible to this phenomenon when punctured with a needle. In retina practice, single-use vials are commonly used in the clinic and include ophthalmic formulations of antivascular endothelial growth factor, anticomplement agents, and intraocular formulations of triamcinolone. Most commonly, these medications are prepared using a large-bore filter needle (18-20 gauge) before the medication is injected intravitreally with a smaller gauge needle (typically 30 gauge or smaller).

To date, there have been no reports of coring within the ophthalmic literature. However, the American Society of Retina Specialists (ASRS) Research and Safety in Therapeutics (ReST) Committee has recently been informed of several coring events associated with a variety of IVT medications (Figure 1). In each case, the physician observed a dark-colored particle within the medication vial rather than within the syringe. In no case was the drug product injected intravitreally, and no safety events have been reported in association with these observations. For the purposes of raising awareness, multiple relevant factors should be considered.

Needle Characteristics

Reports in the nonophthalmic literature have highlighted different needle and cannula characteristics that may influence the likelihood of coring. The adoption of blunt plastic cannulae over sharp stainless steel needles to reduce needlestick injuries may have increased the incidence of coring,[6] a practice that has previously been widely embraced in operating rooms and by anesthesia personnel.[7,8] A prospective study by Wani et al[9] evaluated the

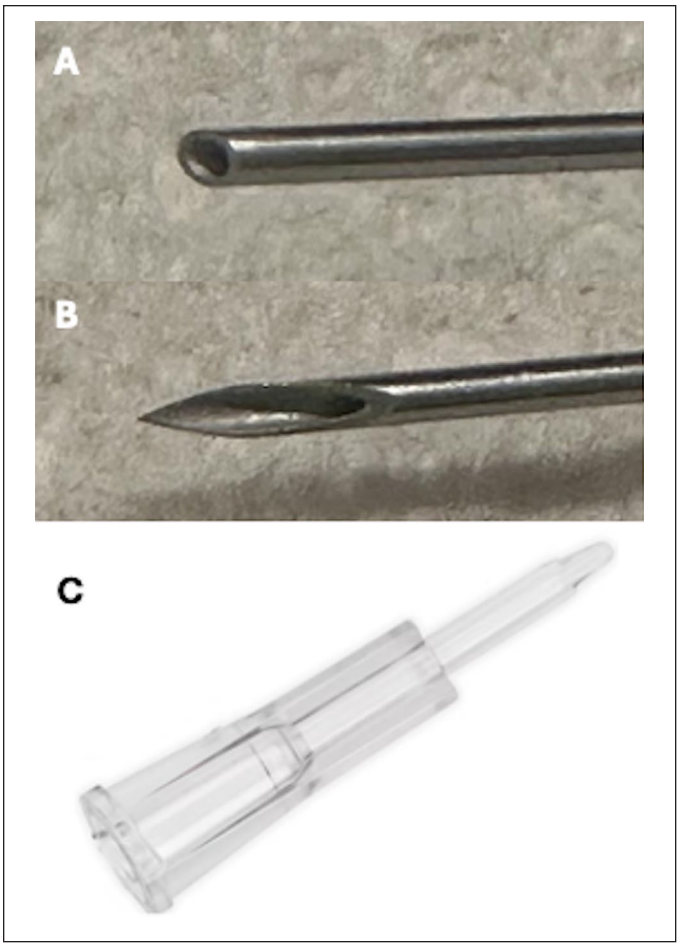

Figure 2. (A) Cross-section of an 18 gauge blunt stainless steel fill needle. (B) Cross-section of an 18 gauge sharp stainless steel hypodermic needle. (C) Cross-section of a blunt plastic filterless cannula.

incidence of coring when blunt plastic filterless safety cannulae were used instead of sharp stainless steel needles (18 gauge) to enter rubber-topped vials and found an incidence rate of 40.8% vs 4.2%, respectively. As such, some institutions have abandoned the use of blunt plastic cannulae for withdrawing liquid medications (Figure 2C).[10]

In retina practice, stainless steel, blunt fill, filter, and beveled 18 or 19 gauge needles are commonly used to draw up IVT medications (Figure 2A). These needles are either stocked separately or included as part of the commercial packaging and injection kits for intraocular medication. Unlike sharp hypodermic needles (Figure 2B), many of these needles lack a cutting edge, enhancing provider safety by reducing the risk of a needlestick injury. To date, there are no known studies comparing the rates of rubber stopper coring in blunt filter needles vs sharp hypodermic filter needles. There are anecdotal reports within the retina community of the occurrence of coring with both types, with both needle types having a non-zero risk. Larger bore needles have also been associated with a higher rate of rubber coring when multi-use vials were tested.[11]

It is important to note that the use of a filter needle (typically 5 μm pore size) eliminates the introduction of particulate matter into the syringe. These filter needles are commonly used in retina practice to prevent transfer of particulate material from a drug vial into the syringe being used to inject the medication, and they are commonly stocked along with IVT drug vials in injection kits. Even though coring is a rare event, its known occurrence emphasizes the importance of using the appropriate filter needle when drawing up IVT medications.

Vial Characteristics

Rubber vial stoppers are a mainstay in medical use, especially for multi-dose, large-volume vials. Multiple punctures through a multi-use vial can more easily produce a rubber core.[11] The rubber stopper material may also play a role in the incidence of coring, including variations in manufacturing of the stopper material. For example, thicker stoppers have been associated with higher rates of coring compared with thinner stoppers.[4] In a small prospective trial, rubber stoppers with larger surface areas were observed to core more often than those with small surface areas.[3] Because of the increased risk of coring in multi-use vials (as well as medication errors and contamination), single-use vials, as are used for IVT medications, are becoming increasingly favored within the broader medical community.

Procedural Considerations

Some studies have concluded that vial puncture at a 45 degree angle can reduce the incidence of coring,[4,12] while another report showed no difference in coring between a 45 degree and 90 degree puncture for the same size and type of needles.[11] It therefore is unclear how significant a role the angle of needle penetration plays in coring incidence.

Existing Recommendations

Coring may be difficult to detect due to the small size of the particles and potential masking from the vial label. Prevention has focused primarily on careful manual inspection of the drug vial before and after needle entry and inspection of the syringe after drawing up the medication, particularly when a filter needle is not used (eg, in preparation of IVT triamcinolone). Additional safeguard measures may include altering the angle of entry into the rubber vial top, controlling the drawing pressure, changing the drawing needle and syringe size, or using a single-use vial vs a multi-use vial. For most IVT injections, a stainless steel filter needle should be used when drawing up single-use medications to prevent the possibility of cored stopper or other particulate material entering the eye. To prevent bacterial contamination of the medication, it is recommended to wipe the vial stopper with alcohol before introducing the filter needle, if indicated on the drug label. In addition, it is important to use any large bore aspiration needles or any small gauge injection needles that are included with the medication kits, as these kits have been created after the review and approval of the US Food and Drug Administration.

Potential Considerations and Implications in Retina Practice

The prescribing information for IVT medication recommends inspecting medication vials and prefilled syringes for particulates before administration. In addition, given the widespread use of stainless steel filter needles for aspiration of medication, as well as the small gauge needles used to perform IVT injections, visible particles are unlikely to be injected intravitreally. It is important to note that no known safety events in the field of retina have been reported in the context of vial coring. If coring is seen, the medication within the vial should be discarded. The use of prefilled syringes, which are more widely available, also eliminates the risk of coring.

Conclusions

The true incidence of coring is unknown in medical practice and, particularly, in ophthalmology. Although the exact incidence of rubber stopper fragmentation in retina practice is not well-documented, there have been no known safety events associated with this phenomenon in the context of intraocular injections. Specific vial stopper characteristics may increase the likelihood of coring, but the introduction of stainless steel filter needles reduces the risk of coring, and prefilled syringes eliminate the risk of introduction of cored material with IVT medication injection.

Given the widespread use of IVT injections for managing a variety of retinal diseases, it is important to raise awareness of coring among retina specialists and allied healthcare personnel so this phenomenon can be recognized when it occurs. Practical measures, such as careful inspection of vials and adherence to best practices during medication preparation, can be helpful to recognize coring before an affected vial is used.

Ethical Approval

Ethical board approval was not required for this study.

Statement of Informed Consent

There were no human participants in this article, and informed consent was not required.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article:
Dr. Ali is a consultant to 4DMT, Allergan/Abbvie, Apellis, Astellas, Eyepoint, Genentech, Ocuphire, Optomed, and Regeneron; is a speaker for Apellis and Astellas; and is an advisory board member of OcuTerra and Orasis.
Dr. Arepalli is a consultant to AbbVie/Allergan, Alimera, and Regeneron.

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Dr. Deaner is a consultant to Alimera, Bausch + Lomb, Eyepoint, Genentech, and Regeneron.
Dr. Jain is a principal investigator for Janssen Pharmaceuticals and Ocugen Inc.
Dr. London is a consultant to Allergan/Abbvie, Appelis, Eyepoint, Genentech/Roche, Ionis Pharmaceuticals, Iveric Bio, and Notal Vision; is a principal investigator for Amgen, Annexon, Boehringer Ingelheim, Clearside Biomedical Inc, Eyepoint, Genentech/Roche, Gyroscope, Ionis Pharmaceuticals, Janssen Pharmaceuticals, Notal Vision, Oculis, OcuTerra Therapeutics, Outlook Pharmaceuticals, Oxurion, and Regeneron.
Dr. Schneider is a consultant to Apellis, Carl Zeiss Meditec, Iveric Bio, Notal Vision, and Regeneron; and is a principal investigator for Carl Zeiss Meditec, Clearside Biomedical Inc, Iveric Bio, Notal Vision, Oculis, OcuTerra Therapeutics, Oxurion, and Regeneron.
Dr. Suner is a consultant to Allergan/Abbvie, ANI/Alimera, Apellis, Astellas, Eyepoint, Genentech, Ocular Therapeutix, and Regeneron; and is a speaker for Apellis, Genentech, and Regeneron.
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Dr. Vajzovic is a consultant to Abbvie/Allergan, Adverum, Alcon, Alimera Sciences, Alkeus, Apellis, Astellas, Bausch + Lomb, Biocryst, Lexitas, Nanoscope, Ocugen, Ocular Therapeutix, OcuTerra, ONL Therapeutics, RegenexBio, and Roche/Genentech; is a principal investigator for Abbvie/Allergan, AGTC, Alcon, Aldeyra, Apellis, Gyroscope, Heidelberg Engineering, Janssen, Novartis, Ocugen, Ocular Therapeutix, RegenexBio, and Roche/Genentech; has a patent with Alcon; and is on the advisory board of Clearside Biomedical.
Dr. Vora is a consultant to Apellis, Eyepoint, Kyoto Drug Discovery and Development, Outlook Therapeutics, and Paradigm Biopharmaceuticals; is a principal investigator for Eyepoint, Kyoto Drug Discovery and Development, Ocular Therapeutix, and Outlook Therapeutics; is a speaker for Iveric Bio; and is an advisor for Apellis, Eyepoint, Genentech, and Regeneron.
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