REVIEW ARTICLE

Cyanoacrylate Glues for Wilderness and Remote Travel Medical Care

Kyle P. Davis, MD; Robert W. Derlet, MD

From the Department of Emergency Medicine, UC Davis School of Medicine, Sacramento, CA (Drs Davis and Derlet).

Cyanoacrylate (CA) glues are commonly used in medical and household repairs. Their chemical compositions have been refined over half a century, making some more suitable than others for creative applications. In remote settings where advanced medical care is not accessible, readily available CAs of differing chemical composition may possess an important therapeutic function. Within this paper we critically examine the published therapeutic risks and benefits of both pharmaceutical and hardware grade CAs when applied in acute care situations. Topics discussed include wound closure as well as the treatment of burns, abrasions, and blisters. Also considered are their chemical properties, toxicities, and potential off-label uses.

Key words: cyanoacrylates, “super glue”, adhesives, Dermabond, lacerations, blisters

Introduction

From the hardened alpinist to the jungle explorer, most backcountry travelers have heard of or experimented themselves with instant adhesive to mend wounds when isolated from definitive medical care. Since their discovery in 1947, cyanoacrylates (CAs) have been used in numerous applications deviating from their intended purpose as a clear resin for gun sights.^{1,2} By 1959, the fast curing and strong adhesive properties had found their way into the medical field when Coover et al³ reported on their applicability to wound closure. Methyl 2-cyanoacrylate (MCA) and to a greater extent, ethyl-2-cyanoacrylate (ECA), are commercially marketed today as hardware-grade instant adhesives.⁴ Early examination of these compounds revealed histotoxic properties, and their use by many medical practitioners was subsequently discontinued. Nevertheless, these off-the-shelf adhesives continue to be used by some healthcare providers for wound repair, hemostasis, and various surgical applications.^{5–7} Longer chain CAs with properties more conducive to medical use have since been developed. Of these, there are currently only a few US Food and Drug Administration (FDA)-approved CAs: 2-octyl cyanoacrylate (OCA, Dermabond) and various formulations of *n*-butyl-2-cyanoacrylates (BCA), some with dye to visualize the applica-

tion (Indermil, TRUFILL, Histoacryl, and Histoacryl Blue). Given the barriers, including cost, availability, and the prescription requirement for medical-grade adhesives, the use of hardware store CAs in underdeveloped settings may be an acceptable therapeutic alternative despite their relative toxicities and differing physical properties. In this paper we describe these differences and explore the therapeutic utility of commercial and medical-grade CA glues in resource-poor and remote locations.

Methods

A comprehensive literature search of MEDLINE, The Cochrane Database, Web of Science, Cinahl, CAB Abstracts, Google Scholar, and BIOSIS through December 2011 was conducted with the oversight of our institution's research librarian. Titles, abstracts, MeSH terms, and key words were searched for the following inclusions: super-glue, crazy-glue, cyanoacrylate(s), tissue adhesive, methyl-cyanoacrylate, ethyl-cyanoacrylate, butyl-cyanoacrylate, and octyl-cyanoacrylate. A single reviewer evaluated all returned English-language abstracts and full-text studies for relevance (ie, pertinence to CA properties, application to wound closure, application to skin problems, antimicrobial effects, adverse effects, and cost). The bibliographies of each of the selected articles were then independently examined for additional publications of pertinence.

Corresponding author: Kyle P. Davis, MD, Department of Emergency Medicine, UC Davis School of Medicine, 2315 Stockton Boulevard, Sacramento, CA 95817.

Figure. Chemical structures of discussed cyanoacrylate glues.

Properties of Cyanoacrylate Glues

Cyanoacrylates are synthesized by condensation of cyano-acetate with formaldehyde in the presence of a catalyst.⁸ The resultant CA monomer is refined and augmented with stabilizers, plasticizers, and other proprietary additives by manufacturers. It is then packaged and distributed in liquid form. During application, the CA is exposed to anionic initiators (eg, hydroxyl groups or lone pairs of electrons on pendant NH_2 groups) on the surfaces being glued, inducing polymerization.^{9,10} The polymer that forms has unique properties that better lend themselves to particular applications (Figure). The utility of the various CAs in the backcountry is directly related to their physical properties. Some of these characteristics include:

- *Wetting, Spreading, and Polymerization*

Wetting and spreading are terms commonly used to describe the interactions of CAs with their binding surface. They are indicative of the affinity and strength between the adhesive and substrate.¹¹ When the CA

spreads, there is more surface available for the nucleophilic initiators to act and an accelerated polymerization results.¹⁰ On proteinaceous surfaces (eg, biologic tissues), higher *n*-alkyl- α -cyanoacrylate homologs (ie, a greater number of CH_2 units in the main carbon chain) wet, spread, and polymerize faster. Methyl, ethyl, and propyl monomers do not spread and consequently take much longer to polymerize. On nonproteinaceous surfaces the reverse was found; lower homologs wet, spread, and polymerize at faster rates.¹² Although this is true of unadulterated CAs, manufacturers have optimized polymerization speeds to better suit their intended purpose. It can be slowed by including a polymerization inhibitor, or sped up by exposing it to an initiator as found in the foam applicator tip of a Dermabond ProPen (2-octylcyanoacrylate).¹³

- *Stability*

During extended travel, it is important that the CA continues to function in extreme environments. Freezing or heat exposure might render the glue useless, while a low flashpoint and high combustibility might allow it to serve as an improvised fire starter. A long shelf life and the ability to use the glue more than once have many obvious benefits. Outlined in the Table are some of the available, representative data on these glues. Properties and recommendations will vary slightly depending on purity of the compounds, additives, and the manufacturer.

Applications in Wound Closure

The medicinal utility of CAs has been the subject of investigation for more than 50 years. Some of the earliest studies from the 1960s and 1970s claimed that the initial tensile strength of wounds closed with MCA and BCA

Table. Representative data on discussed cyanoacrylate glues

Glue	Storage considerations and shelf life	Melting point	Flashpoint	Packaging and reusability
Methyl-CA	Shelf life 1 year. Store in original container, upright in a cool, dry place ⁷⁶	-40°C^{77}	79°C^{77}	Unsterile and reusable
Ethyl-CA (eg, Krazy-Glue)	Store in a cool, dark area and keep tightly sealed ⁷⁸	$< -20^\circ\text{C}^{78}$	75°C^{77}	Unsterile and reusable
<i>n</i> -Butyl-2-cyanoacrylate (eg, Histoacryl)	Expires after 1 year. Manufacturers recommend refrigeration if being stored for >28 days ⁷⁹	Unlisted	$>80^\circ\text{C}^{80}$	Sterile and intended for single use ^{a,79}
2-Octyl cyanoacrylate (eg, Dermabond)	Expires after 2 years, no refrigeration required ⁸¹	Unlisted	$65.6^\circ\text{--}93.3^\circ\text{C}^{82}$	Sterile and intended for single use ⁸¹

^a Cultures from reused vials yielded no growth in one study.⁴³

surpassed that of conventional suture. Additional studies challenged these conclusions.^{14,15} The 1994 examination by Noordzij et al¹⁶ of wound breaking strength using Histoacryl (*N*-butyl-2-cyanoacrylate) and 5-0 polypropylene (simple interrupted stitches) found the Histoacryl closures to be one twelfth as strong as the percutaneous suture after 30 minutes. Breaking strength between the two equalized only after 7 days, when the suture was removed.¹⁶ A year later, a similar study removed the suture on day 7 and the Histoacryl was allowed to fall off on its own before strength testing on day 20. The researchers determined there were no significant differences at this time, when measuring displacement (stretch) and energy absorption (wound strength).¹⁷

Using Nexaband Liquid (OCA), the same conclusion, that suture is initially stronger than CA adhesives, was demonstrated.¹⁸ Furthermore, OCA was proven to have a three-dimensional breaking strength 4 times that of BCA.^{19,20} Singer et al²¹ went a step further, demonstrating that the mechanism of failure for Dermabond was predominantly “interfacial” in nature (the CA film separated from the skin), whereas that of Indermil (BCA) was “cohesive” (the film split/fractured). Their most recent publication concerning wound bursting strengths confirmed that Dermabond is significantly stronger than another BCA (Histoacryl) and both are significantly stronger than Steri-Strips (3M, St. Paul, MN).²² This is consistent with the 2001 findings of the Eisenhower Army Medical Center. Their study found comparable strengths of closure between OCA and interrupted subcuticular 4-0 Monocryl, both of which were superior to Steri-Strips and inferior to staples.²³ A thorough search for the tensile strength afforded by ECA-closed wounds was fruitless. Singer et al^{21,22} assert that the wound bursting strength of ECA is inferior to that of OCA, referencing their 2004 publication. This is logical, as the lower homologs have been proven more brittle, but we were unable to turn up direct evidence in support of this claim.

Applications for Other Skin Problems

Friction blisters, abrasions, and burns are all likely to be encountered at some time on physically demanding excursions. Little evidence for optimal treatment exists in the literature, and CAs should be considered in this realm. It is now well understood that a moist wound environment optimizing humidity, oxygen, and protection from foreign bodies is conducive to healing and pain alleviation.^{24–26} Ostensibly, the protective barrier formed by CAs provides these favorable elements. Unfortunately, we did not encounter any studies including the shorter alkyl chains; this is likely a consequence of early accounts of

their histotoxicity. Nevertheless, there are a few examining various other CAs.

The first reports investigating blister treatment came out of the Letterman Army Institute of Research. They considered *n*-butyl, isobutyl, isoamyl (IACA), pentyl, *n*-heptyl, and trifluoro-isopropyl CAs. After laboratory and field tests, they concluded that the CAs work best over a denuded and raw blister base. They further found IACA to be the most promising as it produced the smallest halo of inflammation, relieved pain, inhibited infection, allowed for the continuation of activity, and almost universally outperformed the control and Neosporin with a bandage.²⁷ Follow-up studies were conducted on intact and abraded skin of rabbits. Use of IACA was shown to be mildly irritating after its initial application. Nearly all IACA could be recovered after 2 weeks, intimating that the irritation resulted from the polymerization reaction and not from the release of toxic metabolites.^{28,29}

As discussed previously, the newer tissue adhesives result in less histotoxicity, and OCA in particular has recently been used to battle blisters. It has been shown to provide an occlusive, healing environment, making it an ideal treatment candidate for this application.^{30,31} In 2006, US soldiers were again recruited to participate in a prospective study examining the treatment of friction blisters on feet. In the standard therapy arm, investigators cleaned the site, removed any denuded skin or drained fluid with a needle if the roof was intact before applying tincture of benzoin, moleskin, and an adhesive bandage. Examiners found increased discomfort during treatment in the OCA arm and no significant difference in patient satisfaction, pain on follow-up, or time to return to activity.³² Given OCA's shortfalls in blister treatment, some have envisioned a preventive role for it. Patents have been filed to use CAs as an artificial callous in blister-prone areas.^{33,34}

When applied to burns and abrasions, OCA's role remains somewhat undefined. Sprayed onto second-degree burns, it resulted in the same reepithelialization and infection rates as Tegaderm.³⁵ In a 2002 study from the University of Miami, Eaglstein et al³⁶ demonstrated the hemostatic and pain-mitigating abilities of Liquid Adhesive Bandage (LAB) on cuts and abrasions. The product was recently approved by the FDA and according to the investigators is more flexible than its OCA counterpart, Dermabond. That said, there was no statistical difference between the wound-healing speed of LAB and a standard adhesive Band-Aid.^{36,37} Another study compared the healing abilities and histotoxicity of LAB with Biobrane when applied to abrasions on guinea pigs. Investigators also found no difference in histopathology or healing times.¹³

Antimicrobial Effects

Early investigations demonstrated that CA films confer antimicrobial properties and that increased growth inhibition was found among the shorter alkyl chains.^{38–40} Shortly afterward, a pattern displaying increased bacteriotoxicity against gram-positive vs gram-negative organisms was revealed. This discovery has led investigators to postulate that the polymerization with hydroxyl groups found in bacterial cell walls is likely responsible for the observed bacteriostatic activity. Thus, the outer lipopolysaccharide capsule surrounding the cell wall of gram-negative microorganisms may impede this action.^{41,42} Quinn et al⁴³ found that the CA polymerization changed the physical properties of the growth agar, which could also account for inhibited growth. In addition to these two mechanisms, the film produced by the cured CA creates a barrier, further preventing infection.⁴⁴ It is important to note the observation by Singer et al^{21,45} that this mechanism of microbial defense is dependent on the integrity of the film. For example, a BCA covering may be compromised merely 1 hour after its application secondary to its brittleness, whereas OCA is significantly more flexible and less likely to crack.

As of late, most studies have focused on the antibacterial effects of OCA. One such examination coated an agar growth medium with Dermabond, allowing it to dry. The film prevented both gram-positive and gram-negative growth, causing the authors to speculate that this is secondary to the impermeability of nutrients essential for growth through the film.² Similar findings were discovered using LAB. The film was found to act as a barrier, protecting wounds from outside infection with *Staphylococcus aureus* (nonmotile) and *Pseudomonas aeruginosa* (highly motile). It also decreased the bacterial load of previously inoculated wounds covered by LAB; hydrocolloid bandages fostered bacterial growth.⁴⁶ In spite of the above, a meta-analysis comprising 5 randomized control trials comparing infection rates between OCA and sutured wound closures showed comparable outcomes.³⁷

A handful of studies have looked at the bacteriologic effects of hardware-grade ECA. They too have been proven bactericidal against gram-positive (including multiresistant strains of *S. aureus*) and, to a lesser extent, gram-negative organisms.^{6,47} Although it does not appear that producers of these glues manufacture them to be sterile, one British study found them to be so, and they could remain sterile if applied properly between multiple patient uses.⁴⁸ This was verified in the United States when clinicians from Carolina's Medical Center reported on 5 readily available ECA adhesives: Bondini (Pro-Tel, Inc, Santa Monica, CA), Krazy glue (Borden, Inc, Co-

lumbus, OH), Quick Tite gel (Loctite Corp, Cleveland, OH), Duro Superglue (Loctite Corp, Cleveland, OH), and Sure Shot (Devcon Corp, Wood Dale, IL). Furthermore, all of the different brands displayed no differences in their ability to prevent bacterial growth after inoculation.⁶

Adverse Effects

Not long after their discovery and subsequent application to medicine, adverse side effects to the short-chain CAs were observed. Histotoxicity, tissue necrosis, and their related sequelae caused the original short-chain alkyl CAs to fall from favor, particularly with the innovation of higher homologs.^{11,28}

Polymerization of the CAs is an exothermic reaction, and higher temperatures are generated among the short-chain esters. Longer chains polymerize more slowly, releasing less heat.^{11,49} Thus, a noted consequence of topically applied short-chain CAs is tissue damage and burns.^{8,50,51} Osmond et al⁵² noted that because of its length, OCA polymerizes at a slower rate, releases less heat, and accordingly should cause less pain with application. Pharmaceutical companies have further refined their CA tissue adhesives to minimize this risk. Most ECA manufacturers simply warn against the potential for mild skin irritation. Yet, the Material Safety Data Sheet of Accumetric's BOSS 181 Cyano-Gel specifically warns against the possibility of a severe exothermic reaction with risk of fire and burns if the glue comes in contact with cotton or wool.⁵³

Cyanoacrylate polymers degrade by hydrolytic scission, resulting in formaldehyde and alkyl-cyanoacetate. Minimizing absorption of these toxic derivatives yields a less necrotizing and more biocompatible product.^{5,54} Via urine analysis and radioactively tagged carbon-14, Ousterhout et al⁵⁵ examined CA absorption through intact skin and split-thickness skin grafts. In both cases, they demonstrated that shorter chain CAs are taken up more quickly, increasing the potential for their acute inflammatory reaction.⁵⁵ Singer et al³⁰ reason that, at least among topically applied FDA-approved tissue adhesives, any significant degradation occurs after the adhesive film has sloughed off. Numerous studies have examined the tissue histology after topical, intradermal, and subcutaneous CA exposure. Since the 1960s, the general consensus has remained that a more acute and severe cytotoxic reaction occurs among tissue exposure to the lower homologs.^{5,15,51,56–59} Yet, for wound closure and various other procedures, there have been a considerable number of studies finding histologic equivalence between ECA and more widely accepted modalities of repair.^{7,49,60–66} Recently published case reports

both in support of the medical application of ECA^{6,67,68} and against its use^{69–71} continue to foster the debate.

Cost

As outlined above, FDA-approved tissue adhesives have many properties that make them a good alternative to more established medical procedures. A number of studies have touched on the fiscal benefits afforded by CAs, and almost all of these have been on the subject of wound closure. Osmond et al⁷² performed a cost-minimization analysis looking specifically at pediatric facial lacerations. Accounting for the expenses associated with equipment utilization, healthcare worker time, and so on, they found that the glue provided significant savings vs suture. The upfront cost may be more expensive than most suture, but the vast majority of studies maintain that CA repairs, using ECA or FDA-approved tissue adhesives, are more cost-effective than their equivalent non-CA substitutes.^{7,30,64,73,74} Cost reduction is further attributed to a decreased need for supplemental materials such as suture kits, and revision secondary to infection or dehiscence.³⁷ Levy et al³² reason that the relatively high manufacturer's suggested retail price of Dermabond may be justifiable to backcountry adventurers and military personnel as a precautionary addition to their first aid kits. In 1993 Matthews⁴⁸ showed a 28% cost savings in using a commercially available CA compared with its medically purposed CA counterpart. Another study found an ECA-based remedy to cost merely 1.5% that of Histoacryl.⁷⁵

Discussion

In remote settings, several factors must be weighed when choosing between commercial and medicinally purposed CA glues. These include the expected purpose of the adhesive, alternative modalities of repair, side effects, and cost. Today's commercially produced instant glues have long been associated with deleterious effects, causing many practitioners to shy away from their use within medicine. The published literature reveals more undesirable consequences with their application compared with newer pharmaceutical-grade tissue adhesives. Within the laboratory setting, the lower homologs have been shown to cause localized inflammation, release toxic metabolites more quickly, and possess inferior physical properties for tissue adhesion. That being said, these drawbacks are relative and although the commercial glues fall short of the standards set by their pharmaceutical counterparts, they still have a proven role. As reviewed above, a considerable number of clinicians reported on the successful use of short-chain CAs for various acute care

fixes without complication. There are likely many more successful therapeutic repairs away from the hospital that go unreported.

Within wilderness medicine, adventure travel, and medical practice in frontier settings, the treatment of friction blisters, abrasions, burns, lacerations, and hemorrhage are just a few of the proposed therapeutic roles of CAs. Both BCA and OCA are proven modalities of wound closure, although reports are mixed regarding efficacy of closures using over-the-counter glues. The superiority of OCA over routine blister, abrasion, and burn care has not been clearly demonstrated, and there is a paucity of studies on these subjects using off-the-shelf glues. However, both short- and long-chain CAs are promising as antimicrobial and protective barriers that aid in wound healing and, to some extent, pain mitigation. The lower cost associated with CA application compared with conventional treatments adds to their appeal.

Properties of the ideal CA are largely user dependent. A well-funded individual tasked with providing healthcare in isolated settings might be better served carrying an FDA-approved tissue adhesive. The avid outdoorsman, whose pack is as light as his wallet, might prefer a tube of Super Glue for commonly encountered field equipment repairs and infrequent therapeutic use. Overseas, access to pharmaceuticals may be limited, influencing a practitioner's treatment preference. We believe that when applied judiciously, in the same fashion as FDA-approved tissue glues, the hardware store CA instant adhesives can be used in a relatively safe and efficacious manner. Additional studies comparing the therapeutic utilization of different off-the-shelf glues are needed. Similarly we do not know the proprietary manufacturing additives that differentiate them and thus cannot make any specific brand recommendations or attestations to their safety. Consequently, we recommend cautiously using these glues in situations when no FDA-approved alternative is feasible. Ultimately, the best CA relies on its intended purpose and proper application, but there exist several closely related alternatives that will more than suffice.

References

1. Ardis AE, inventor; B.F. Goodrich Company, assignee. Preparation of Monomeric Alkyl Alpha-Cyano-Acrylates. United States Patent 2467926. April 19, 1949.
2. Gooch JW. *Biocompatible Polymeric Materials and Techniques for Wounds*. 1st ed. New York, NY: Springer; 2010.
3. Coover HW, Joyner FB, Shearer NH, Wicker TH. Chemistry and performance of cyanoacrylate adhesives. *J Soc Plast Surg Eng*. 1959;15:413–417.

4. Cummins KJ. Methyl 2-Cyanoacrylate (MCA) Ethyl 2-Cyanoacrylate (ECA). 1985. Available at: <http://www.osha.gov/dts/sltc/methods/organic/org055/org055.html>. Accessed November 13, 2011.
5. Toriumi DM, Raslan WF, Friedman M, Tardy ME. Histotoxicity of cyanoacrylate tissue adhesives: a comparative study. *Arch Otolaryngol Head Neck Surg.* 1990;116:546–550.
6. Robicsek F, Rielly JP, Marroum MC. The use of cyanoacrylate adhesive (Krazy Glue) in cardiac surgery. *J Card Surg.* 1994;9:353–356.
7. Marques dos Santos CH, Rodrigues LL, Matos FBM. Ethyl-cyanoacrylate use for skin closure in patients subjected to laparoscopic cholecystectomy. *Afr J Pharm Pharmacol.* 2011;1:30–32.
8. Leggat PA, Smith DR, Kedjarune U. Surgical applications of cyanoacrylate adhesives: a review of toxicity. *ANZ J Surg.* 2007;77:209–213.
9. Pawar RP, Jadhav AE, Tathe SB, Khade BC, Domb AJ. Medicinal applications of cyanoacrylate. In: Domb AJ, Kumar N, eds. *Biodegradable Polymers in Clinical Use and Clinical Development*. 1st ed. Hoboken, NJ: John Wiley and Sons; 2011:417–449.
10. Matsumoto T, Pani K, Hardaway RM, Leonard F. N-alkyl-a-cyanoacrylate monomers in surgery: speed of polymerization and method of their application. *Arch Surg.* 1967;94:153–156.
11. Leonard F, Kulkarni RK, Nelson J, Brandes G. Tissue adhesives and hemostasis-inducing compounds: the alkyl cyanoacrylates. *J Biomed Mater Res.* 1967;1:3–9.
12. Leonard F, Hodge JW Jr, Houston S, Ousterhout DK. α -Cyanoacrylate adhesive bond strengths with proteinaceous and nonproteinaceous substrates. *J Biomed Mater Res.* 1968;2:173–178.
13. Quinn J, Lowe L, Mertz M. The effect of a new tissue-adhesive wound dressing on the healing of traumatic abrasions. *Dermatology.* 2000;201:343–346.
14. Heis W, Guthy E, Faul P. Comparative studies of tensile strength in wound treated with adhesive and by suture. Symposium on Adhesives in Surgery; Sep 1–2, 1967; Vienna.
15. Lamborn PB Jr, Soloway HB, Matsumoto T, Aaby GV. Comparison of tensile strength of wounds closed by sutures and cyanoacrylates. *Am J Vet Res.* 1970;31:125–130.
16. Noordzij JP, Foresman PA, Rodeheaver GT, Quinn JV, Edlich RF. Tissue adhesive wound repair revisited. *J Emerg Med.* 1994;12:645–649.
17. Yaron M, Halperin EM, Huffer W, Cairns C. Efficacy of tissue glue for laceration repair in an animal model. *Acad Emerg Med.* 1995;2:259–263.
18. Bresnahan KA, Howell JM, Wizorek J. Comparison of tensile strength of cyanoacrylate tissue adhesive closure of lacerations versus suture closure. *Ann Emerg Med.* 1995;26:575–578.
19. Perry L. An evaluation of acute incisional strength with traumaseal surgical tissue adhesive wound closure. Leonia, NJ: Dimensional Analysis Systems Inc; 1995.
20. Quinn J, Wells G, Sutcliffe T, et al. A randomized trial comparing octylcyanoacrylate tissue adhesive and sutures in the management of lacerations. *JAMA.* 1997;277:1527–1530.
21. Singer AJ, Zimmerman T, Rooney J, Cameau P, Rudomen G, McClain SA. Comparison of wound-bursting strengths and surface characteristics of FDA-approved tissue adhesives for skin closure. *J Adhesion Sci Technol.* 2004;18:19–27.
22. Taira BR, Singer AJ, Rooney J, Steinhaff NT, Zimmerman T. An in-vivo study of the wound-bursting strengths of octyl-cyanoacrylate, butyl-cyanoacrylate, and surgical tape in rats. *J Emerg Med.* 2010;38:546–551.
23. Shapiro AJ, Dinsmore RC, North JH Jr. Tensile strength of wound closure with cyanoacrylate glue. *Am Surg.* 2001;67:1113–1115.
24. Hinman CD, Maibach H. Effect of air exposure and occlusion on experimental human skin wounds. *Nature.* 1963;200:377–378.
25. Winter GD. Formation of the scab and the rate of epithelialization of superficial wounds in the skin of the young domestic pig. *Nature.* 1962;193:293–294.
26. Pollack S. Wound healing: a review. III. Nutritional factors affecting wound healing. *J Dermatol Surg Oncol.* 1979;5:615–619.
27. Akers WA, Leonard F, Ousterhout DK, Cortese TA Jr. Treating friction blisters with alkyl- $\{\alpha\}$ -cyanoacrylates. *Arch Dermatol.* 1973;107:544–547.
28. Arthaud LE, Lewellen GR, Akers WA. The dermal toxicity of isoamyl-2-cyanoacrylate. *J Biomed Mater Res.* 1972;6:201–214.
29. Akers WA. Annual progress report, FY 1972. Letterman Army Institute of Research. 1972; RCS SGRD-288(RI).
30. Singer AJ, Quinn JV, Hollander JE. The cyanoacrylate topical skin adhesives. *Am J Emerg Med.* 2008;26:490–496.
31. Singer AJ, Nable M, Cameau P, Singer DD, McClain SA. Evaluation of a new liquid occlusive dressing for excisional wounds. *Wound Repair Regen.* 2003;11:181–187.
32. Levy PD, Hile DC, Hile LM, Miller MA. A prospective analysis of the treatment of friction blisters with 2-octylcyanoacrylate. *J Am Podiatr Med Assoc.* 2006;96:232–237.
33. Barley LV Jr, inventor; Medlogic Inc, assignee. Methods for retarding blister formation by use of cyanoacrylate adhesives. United States Patent 5,306,490. April 26, 1994.
34. Greff RJ, Tighe PJ, Byram MM, Barley LV, inventor; Medlogic Global Corp, assignee. Cyanoacrylate adhesive compositions. United States Patent 6,191,202. Feb. 20, 2001.
35. Singer AJ, Mohammad M, Thode HC Jr, McClain SA. Octylcyanoacrylate versus polyurethane for treatment of burns in swine: a randomized trial. *Burns.* 2000;26:388–392.
36. Eaglstein WH, Sullivan TP, Giordano PA, Miskin BM. A liquid adhesive bandage for the treatment of minor cuts and abrasions. *Dermatol Surg.* 2002;28:263–267.

37. Singer AJ, Thode HC Jr. A review of the literature on octylcyanoacrylate tissue adhesive. *Am J Surg*. 2004;187:238–248.
38. Fasset DW, Rondabush RL, Emley IC, Graulich LB. Microbiological growth from Eastman No. 910 Monomer and adhesive. *Cohesive News*. 1961;1:5.
39. Awe WC, Roberts W, Braunwald NS. Rapidly polymerizing adhesive as a hemostatic agent: study of tissue response and bacteriological properties. *Surgery*. 1963;54:322–328.
40. Lehman RAW, West RLEE, Leonard F. Toxicity of alkyl 2-cyanoacrylates: II. Bacterial growth. *Arch Surg*. 1966;93:447–450.
41. Eiferman RA, Snyder JW. Antibacterial effect of cyanoacrylate glue. *Arch Ophthalmol*. 1983;101:958–960.
42. Jandinski J, Sonis S. In vitro effects of isobutyl cyanoacrylate on four types of bacteria. *J Dent Res*. 1971;50:1557–1558.
43. Quinn JV, Osmond MH, Yurack JA, Moir PJ. N-2-butylcyanoacrylate: risk of bacterial contamination with an appraisal of its antimicrobial effects. *J Emerg Med*. 1995;13:581–585.
44. Aksoy M, Turnadere E, Ayalp K, Kayabali M, Ertugrul B, Bilgic L. Cyanoacrylate for wound closure in prosthetic vascular graft surgery to prevent infections through contamination. *Surg Today*. 2006;36:52–56.
45. Singer AJ, Hollander JE. *Lacerations and Acute Wounds: An Evidence-Based Guide*. 1st ed. Philadelphia, PA: FA Davis; 2003.
46. Mertz PM, Davis SC, Cazzaniga AL, Drosou A, Eaglstein WH. Barrier and antibacterial properties of 2-octyl cyanoacrylate-derived wound treatment films. *J Cutan Med Surg*. 2003;7:1–6.
47. de Almeida Manzano RP, Naufal SC, Hida RY, Guarnieri LO, Nishiwaki-Dantas MC. Antibacterial analysis in vitro of ethyl-cyanoacrylate against ocular pathogens. *Cornea*. 2006;25:350–351.
48. Matthews SC. Tissue bonding: the bacteriological properties of a commercially-available cyanoacrylate adhesive. *Br J Biomed Sci*. 1993;50:17–20.
49. Kaplan M, Bozkurt S, Kut MS, Kullu S, Demirtas MM. Histopathological effects of ethyl 2-cyanoacrylate tissue adhesive following surgical application: an experimental study. *Eur J Cardiothorac Surg*. 2004;25:167–172.
50. Clarke TF. Cyanoacrylate glue burn in a child—lessons to be learned. *J Plast Reconstr Aesthet Surg*. 2011;64:e170–173.
51. Woodward SC, Herrmann JB, Cameron JL, Brandes G, Pulaski EJ, Leonard F. Histotoxicity of cyanoacrylate tissue adhesive in the rat. *Ann Surg*. 1965;162:113–322.
52. Osmond MH, Quinn JV, Sutcliffe T, Jarmuske M, Klassen TP. A randomized, clinical trial comparing butylcyanoacrylate with octylcyanoacrylate in the management of selected pediatric facial lacerations. *Acad Emerg Med*. 1999;6:171–177.
53. BOSS 181 Cyano-Gel; Material Safety Data Sheet No. 07085850. Elizabethtown, KY: Accumetric, LLC; August 14, 2000. Available at: <http://www.accumetricinc.com/uplimg/boss/msds/181.pdf>. Accessed October 10, 2011.
54. Leonard F, Kulkarni RK, Brandes G, Nelson J, Cameron JJ. Synthesis and degradation of poly (alkyl α -cyanoacrylates). *J Appl Polymer Sci*. 1966;10:259–272.
55. Ousterhout DK, Gladieux GV, Leonard F. Cutaneous absorption of N-alkyl α -cyanoacrylate. *J Biomed Mater Res*. 1968;2:157–163.
56. Thumwanit V, Kedjarune U. Cytotoxicity of polymerized commercial cyanoacrylate adhesive on cultured human oral fibroblasts. *Aust Dent J*. 1999;44:248–252.
57. Zumpano BJ, Jacobs LR, Hall JB, Margolis G, Sachs E Jr. Bioadhesive and histotoxic properties of ethyl-2-cyanoacrylate. *Surg Neurol*. 1982;18:452–457.
58. Tseng YC, Hyon SH, Ikada Y, Shimizu Y, Tamura K, Hitomi S. In vivo evaluation of 2-cyanoacrylates as surgical adhesives. *J Appl Biomater*. 1990;1:111–119.
59. Kline DG, Hayes GJ. An experimental evaluation of the effect of a plastic adhesive, methyl 2-cyanoacrylate, on neural tissue. *J Neurosurg*. 1963;20:647–654.
60. Rickett T, Li J, Patel M, Sun W, Leung G, Shi R. Ethylcyanoacrylate is acutely nontoxic and provides sufficient bond strength for anastomosis of peripheral nerves. *J Biomed Mater Res A*. 2009;90:750–754.
61. Moretti Neto RT, Mello I, Moretti ABS, Robazza CRC, Pereira AAC. In vivo qualitative analysis of the biocompatibility of different cyanoacrylate-based adhesives. *Braz Oral Res*. 2008;22:43–47.
62. Vanholder R, Misotten A, Roels H, Matton G. Cyanoacrylate tissue adhesive for closing skin wounds: a double blind randomized comparison with sutures. *Biomaterials*. 1993;14:737–742.
63. de Azevedo CL, Marques MM, Bombana AC. Cytotoxic effects of cyanoacrylates used as retrograde filling materials: an in vitro analysis. *Pesqui Odontol Bras*. 2003;17:113–118.
64. Gulalp B, Seyhan T, Gursoy S, Altinors MN. Emergency wounds treated with cyanoacrylate and long-term results in pediatrics: a series of cases; what are the advantages and boards? *BMC Res Notes*. 2009;2:132.
65. Landegren T, Risling M, Brage A, Persson JKE. Long-term results of peripheral nerve repair: a comparison of nerve anastomosis with ethyl-cyanoacrylate and epineural sutures. *Scand J Plast Reconstr Surg Hand Surg*. 2006;40:65–72.
66. Saska S, Gaspar AMM, Hochuli-Vieira E. Cyanoacrylate adhesives for the synthesis of soft tissue [in Portuguese]. *An Bras Dermatol*. 2009;84:585–592.
67. Yilmaz C, Kuyurtar F. Fixation of a talar osteochondral fracture with cyanoacrylate glue. *Arthroscopy*. 2005;21:1009.
68. Negri MR, Panzarini SR, Poi WR, Sonoda CK, Manfrin TM, Vendrame dos Santos CL. Use of a cyanoacrylate ester adhesive for splinting of replanted teeth. *Dent Traumatol*. 2008;24:695–697.

69. Wang AA, Martin CH. Full-thickness skin necrosis of the fingertip after application of superglue. *J Hand Surg Am*. 2003;28:696–698.
70. Cascarini L, Kumar A. Case of the month: Honey I glued the kids: tissue adhesives are not the same as “superglue”. *Emerg Med J*. 2007;24:228–229.
71. Belsito DV. Contact dermatitis to ethyl-cyanoacrylate-containing glue. *Contact Dermatitis*. 1987;17:234–236.
72. Osmond MH, Klassen TP, Quinn JV. Economic comparison of a tissue adhesive and suturing in the repair of pediatric facial lacerations. *J Pediatr*. 1995;126:892–895.
73. Goktas N, Karcioğlu Ö, Coskun F, Karaduman S, Menderes A. Comparison of tissue adhesive and suturing in the repair of lacerations in the emergency department. *European Eur J Emerg Med*. 2002;9:155–158.
74. Messi G, Canciani G, Marchi AG. Costs and benefits of the use of tissue adhesives in wounds in children [in Italian]. *Pediatr Med Chir*. 1990;12:185–188.
75. Lin JC, Lin CW, Lin XZ. In vitro and in vivo studies for modified ethyl cyanoacrylate regimens for sclerotherapy. *J Biomed Mater Res*. 2000;53:799–805.
76. Methyl cyanoacrylate adhesives; Material Safety Data Sheet No. 804000N063185; Alpharetta, GA: Chemence, Inc; August 30, 2001. Available at: <http://www.njiai.org/Cyanoacrylate-msd.pdf>. Accessed December 6, 2011.
77. Cary R. *Methyl cyanoacrylate and ethyl cyanoacrylate*. Geneva, World Health Organization; 2001. Concise International Chemical Assessment Document 36. Available at: <http://www.inchem.org/documents/cicads/cicads/cicad36.htm>. Accessed August 23, 2012.
78. Krazy Glue All Purpose; Material Safety Data Sheet No. KG0583; Columbus, OH: Elmer's Products Inc; October 9, 2006. Available at: http://www.krazyglue.com/products/msds/mkg0583_a.htm. Accessed October 19, 2011.
79. Histoacryl topical skin adhesive brochure. 2011 package insert and product brochure. B Braun Corp. Available at: <http://www.tissueeal.com/>. Accessed December 6, 2011.
80. Indermil Tissue Adhesive; Material Safety Data Sheet No. 8886-028275; Mansfield MA: Tyco Healthcare; September 22, 1998. Available at: http://www.kendallhq.com/catalog/MSDS/IndermilTissueAdhesive_2-2004.pdf. Accessed December 6, 2011.
81. Ethicon. 510(k) Premarket Notification K100423. 2010. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf10/K100423.pdf. Accessed December 6, 2011.
82. Dermabond Topical Skin Adhesive; Material Safety Data Sheet No. CLLQF; Somerville NJ: Ethicon Inc; September 4, 1998. Available at: <http://hazard.com/msds/f2/c11/c11qf.html>. Accessed December 6, 2011.