tion during operation is one that minimizes cuff-tracheal surface contact area, if the incidence of postoperative sore throat is to be reduced.

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Comparison of Compounds Used for Intradermal Anesthesia

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Lidocaine and procaine, the local anesthetics most commonly used for intradermal anesthesia, cause considerable discomfort upon injection. Physiologic saline solution has been said to be a satisfactory local anesthetic that is free of discomfort.† This study compares various compounds used for intradermal injection with regard to discomfort and to intensity and duration of anesthesia. The intent was to determine which drug provides the highest patient acceptability and the best anesthesia.

METHOD
A randomized, double-blind study was carried out with 20 adult volunteers serving as their own controls after approval from the Human Studies Committee. Sixteen men and four women, ranging in age from 19 to 45 years and in weight from 54 to 95 kg, participated. None was taking analgesics, sedatives, or tranquilizers. All were considered A.S.A. physical status I.

Six solutions were prepared for each subject in single-dose 1-ml ampules: physiologic saline solution; physiologic saline solution with 0.9 per cent benzyl alcohol; lidocaine, 0.5 per cent; lidocaine, 0.5 per cent, with 0.1 per cent methylparaben; lidocaine, 1 per cent; procaine 1 per cent. No other additive was present. Water was the diluent for the local anesthetics.

The dorsum of each hand was cleansed with isopropyl alcohol and allowed to dry. Using a 1-ml syringe with a 25-gauge needle, an intradermal wheel was raised with 0.1 ml of each test solution, three wheels per hand. The order of drug injections was randomized. Subjects were sitting and did not observe the injections.

Once the needle was in place, the subject was instructed to describe the degree of discomfort and the sensation caused by raising the wheel. Discomfort was rated from 0 (no discomfort) to 2 (severe discomfort).

Anesthesia produced by the wheel of intradermal drug was tested by pin prick, initially 15 seconds after injection and at intervals thereafter to a total duration of 20 minutes. It was rated 0 (no anesthesia) to 3 (excellent anesthesia). Injection sites were observed for adverse local effects.

Initial analysis by a two-way analysis of variance at measured values by subject and drug showed significant variation among subjects. Therefore, the data were adjusted; to eliminate individual variability and then analyzed by ordinary one-way analysis of variance with a priori and a posteriori contrasts to examine differences between specific drugs.

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† The basic two-way analysis of variance model was

\[ M_i = u + S_i + A_i + E_{ij} \]

where \( M_i \) is an observed score for subject \( i \) given drug \( j \); \( u \) is the grand mean; \( S_i \) is subject \( i \)'s mean deviation from \( u \); \( A_i \) is drug \( j \)'s mean deviation from \( u \); and \( E_{ij} \) is the error term. The transformation was made by defining

\[ M_i' = M_i - S_i \]

so that the one-way model became

\[ M_i' = u + A_i + E_{i} \]
Whenever discomfort was experienced with any drug, it was described as a burning, stinging sensation.

Anesthesia produced by all compounds in the first 2 minutes after injection was rated good to excellent (anesthesia scores 2 to 3) except for physiologic saline solution, $P < .001$ (fig. 2). The latter produced poor to no anesthesia (scores 1 to 0) in 85 per cent of subjects. Satisfactory anesthesia began to dissipate after 2 to 3 minutes with benzyl alcohol—saline solution, after 5 minutes with procaine, and after 20 minutes with the lidocaine preparations (fig. 2). Methylparaben did not alter the duration or intensity of anesthesia.

Reactions, consisting of localized itching, erythema, and pseudopod formation, appeared in eight of 20 subjects given procaine, but in no other subject.

RESULTS

Physiologic saline solution with 0.9 per cent benzyl alcohol caused significantly less discomfort on intradermal injection than any other drug tested, $P < .001$ (fig. 1). No discomfort was reported by 85 per cent of subjects, following benzyl alcohol—saline solution injection, whereas absence of discomfort occurred in no more than 15 per cent of subjects with the other compounds studied. Injection of physiologic saline solution alone caused the greatest discomfort. Methylparaben preservative in lidocaine multidose vials did not alter the incidence of discomfort.

DISCUSSION

The anesthesiologist requires intradermal anesthesia only for the brief period when large needles are passed through the sensitive dermis. The ideal drug for this purpose would provide good anesthesia for several minutes, be free of pain on injection, and be devoid of local toxicity as well as the danger of sensitivity.

All drugs tested in the present study caused moderate to severe discomfort on injection except saline solution that contained the preservative benzyl alcohol.

As expected, this study demonstrated that lidocaine and procaine provide good anes-
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The duration of anesthesia with lidocaine exceeded that produced by procaine, but both far exceeded the few minutes needed in most situations in clinical anesthesia. In contrast to saline solution alone, saline solution with benzyl alcohol gave good anesthesia for 2 minutes.

Benzyl alcohol, the bacteriostatic compound in multidose vials of physiologic saline solution, has been known to have anesthetic properties since 1918. Indeed, solutions of 1 to 4 per cent benzyl alcohol have been used as an infiltration anesthetic for various surgical procedures, and a 4 per cent ointment has been employed for topical anesthesia of mucous membranes. High concentrations of benzyl alcohol (5 to 10 per cent) in almond oil cause local tissue damage, but lower concentrations (1 to 4 per cent) in non-oil vehicle are as safe as other local anesthetics. In animal studies, the systemic toxicity of benzyl alcohol is less than that of many other local anesthetics. It is believed to be equally safe in man: to our knowledge, no untoward reaction has been reported.

While adverse reactions to local anesthetics are infrequent and true allergy rare, both do occur. These reactions are limited primarily to the ester-linked type, of which procaine is the most frequent offender. Methylparaben, the preservative in multidose vials of amide-linked local anesthetics (e.g., lidocaine), has been said to be capable of producing severe local and systemic hypersensitivity reactions. In fact, occasional allergic reactions ascribed to lidocaine have been subsequently found to be due to methylparaben. Methylparaben, a derivative of parahydroxybenzoic acid, is chemically related to procaine. Cross-sensitivity between these two drugs may therefore be anticipated. As an aromatic alcohol, benzyl alcohol differs structurally from other anesthetics and methylparaben. It therefore offers an alternative to the clinician wishing to avoid exposure of patients scheduled for minor procedures to potential allergens.

Physiologic saline solution alone causes severe pain on injection and provides no anesthesia, despite claims to the contrary.

In conclusion, physiologic saline solution with 0.9 per cent benzyl alcohol provides good intradermal anesthesia of sufficient duration for many procedures anesthesiologists perform, and produces less discomfort on injection than any other drug. Because of low toxicity, low allergic potential, low cost, and ready availability in sodium chloride multidose vials, this forgotten drug is a useful compound for the anesthesiologist. For more prolonged anesthesia, lidocaine continues to be the drug of choice.

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