Effect of Hepatitis B Vaccine Temperature on Injection Pain

By

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A Master's Research Project

Presented to

Oregon Health Sciences University

School of Nursing

in partial fulfillment

of the requirements for the degree of

Master of Science

June 5, 1996

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ACKNOWLEDGEMENTS

I would like to gratefully acknowledge Roberta S. Erickson, Ph.D., R.N. for her unquestionable willingness to be my research advisor and to guide me through the research process to the completion of an exciting and challenging project in a relatively short period of time. With generosity she shared her knowledge and expertise, and taught me how to perform quality research and to report it in a precise and scholarly manner. Her ability to motivate was exceptional and her support invaluable.

I would also like to thank Una Beth Westfall, Ph.D., R.N. for her support and very valuable assistance as a member of my research committee. Her statistical knowledge and logical approach to any questions that arose during this project has motivated my ability to think critically and has expanded my knowledge.

Furthermore, I would like to thank Vivian Gedaly-Duff, D.N.Sc., R.N. as an important member of my research committee. Her expertise in the field of pain of which she shared generously has contributed enormously to my learning experience.

To Joyce Crane, Ph.D., R.N., my academic advisor, I would like to express my appreciation as she was always there to guide me in decisions I needed to make during the graduate program and to give me support through some very rough times.

To my husband, Niels Krabbe, I am deeply indebted as he spent countless hours in front of the computer to learn the American Psychology Association format and compose tables and figures. His patience and expertise were invaluable in the success of this project.

In conclusion, I would like to acknowledge the employees at the three study sites, the VA Employee Health Clinic, Portland, OR, the OHSU Employee Health Clinic, Portland, OR, and Clark College Health Services, Vancouver, WA for their excitement for and support of this project, and for my co-workers who allowed me time off to complete it.

ABSTRACT

TITLE: Effect of Hepatitis B Vaccine Temperature on Injection Pain

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Nurses have tried different strategies to decrease or eliminate pain and unpleasantness associated with intramuscular injections. Among these strategies are use of different injection sites and techniques, such as muscle relaxation, subject distraction, pre-injection pressure at the site, and topical application of cold. In this study, the effect of two temperatures of injected hepatitis B vaccine, cool (approximately 9.4°C [49°F] and room temperature (approximately 22.8°C [73°]), on the experienced pain intensity and unpleasantness of injection pain at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection was investigated using 100 mm visual analogue scales.

The sample, which was obtained from three health clinics, consisted of 64 subjects who received hepatitis B vaccine injections. The subjects were 19-72 years old (mean 36.3 ± 12.9) and included 22 males and 44 females. The subjects were randomized into two treatment groups. Group I consisted of 11 males and 22 females who received cool hepatitis B vaccine. Group II consisted of 10 males and 21 females who received room temperature vaccine. All subjects received a 1-ml dose of vaccine containing 20 mcg of hepatitis B surface antigen by intramuscular injection in either left or right deltoid muscle.

The two study groups were compared for equivalence in regard to background variables. Qualitative variables (demographic characteristics and past problems with injections) were compared using the chi-square and Fisher's exact test. Quantitative variables (age, number of intramuscular injections in the past year, and injection number in the hepatitis B vaccine series) were compared with two-sample t-tests. No statistically significant differences were found for any of the background variables. Therefore, the groups were considered to be equivalent. Visual analogue scores for pain intensity and unpleasantness at the four rating times were compared using the Mann-Whitney U test. The group that received cool vaccine had a small, but statistically higher pain intensity rating at 5 seconds post injection ($p = .01$). The median rating in this group was 6.0 mm and 1.5 mm in the group that received room temperature vaccine. The respective mean ratings (± SD) were higher, 11.3 ± 13.3 and 5.1 ± 7.7, respectively, due to the positively skewed distribution. At the later ratings (1 minute, 5 minutes, and 10 minutes), the differences were negligible. Of interest is the finding that approximately 1 in 5 subjects who received cool vaccine rated pain intensity at 5 seconds above 20 mm, while only a single subject who received room temperature vaccine had a rating this high. No statistical significance was found between the two groups for reported unpleasantness of injection pain at any of the four rating times.

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CHAPTER I

INTRODUCTION

Statement of Problem

According to the Centers for Disease Control and Prevention (CDC), the incidence of reported cases of acute hepatitis B has increased over the past decade despite introduction of the hepatitis B vaccine (1991). Currently, the strategy for hepatitis B prevention is to vaccinate all individuals at high risk of infection. For the vaccine to have an impact on the spread of the disease, universal vaccination of infants and adolescents has been suggested as a possible measure in this direction (CDC, 1991). Millions of hepatitis B vaccine doses have been administered to date, and millions more will be administered in the future. Generally, the vaccine is well tolerated. The most common reported adverse reaction is pain at the injection site (SmithKline Beecham Pharmaceuticals, 1995).

Hepatitis B vaccine is administered by intramuscular injection, a procedure frequently implemented by nurses. As with some other vaccines, pharmaceutical companies recommend that hepatitis B vaccine be stored in a refrigerator at 2 to 8°C (35 to 46°F) (Merck Sharp & Dohme, 1995; SmithKline Beecham Pharmaceuticals, 1995). Storage above and below the recommended temperature range may reduce vaccine potency. For example, hepatitis B vaccine should not be frozen. Before administration, hepatitis B vaccine is taken out of the refrigerator and injected after varying periods of time. Although the injected vaccine is often cool, the exact temperature of the solution is unknown and probably variable. In anecdotal observations at a college student health center, students who received cool hepatitis B vaccine seemed to report more injection pain than those who received a warmer solution. This raised the question of whether the temperature of the injected vaccine made a difference in the individual's perception of injection pain.

Purpose of Study

The purpose of this study was to compare the effect of two temperatures of injected hepatitis B vaccine, cool (approximately 9.4°C [49°F]) and room temperature (approximately 22.8°C [73°F]) on the perceived intensity and unpleasantness of injection pain at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection. Pain intensity was defined as the amount of pain experienced by the individual. Pain unpleasantness was defined as the extent to which the pain bothered the individual.

Significance to Nursing

For years, nurses have tried different strategies to decrease or eliminate discomfort and pain associated with intramuscular injections. Among these strategies are different injection sites and techniques, e.g., the Z-track technique, muscle relaxation, subject distraction, as well as mechanical methods such as pre-injection pressure at the injection site, and topical application of cold. This study helped to determine whether the temperature of the injected solution is a factor that can make a difference in the intensity and unpleasantness of injection pain.

CHAPTER II

REVIEW OF LITERATURE AND CONCEPTUAL FRAMEWORK

The literature review begins with a description of external cold as a noxious stimulus of pain. The major focus is on injection pain and strategies to decrease or eliminate it. The review includes studies of both adults and children because of the limited research in this area. Studies conducted on the heat stability of hepatitis B vaccine are examined. The Gate Control Theory and the physiology of pain receptors are explored as the conceptual framework for this study.

External Cold and Pain

Pain is difficult to study, in part because of its subjective nature. The International Association for Study of Pain has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (1979, p. 250). Pain is both a distinct sensation of actual or potential tissue damage as well as the individual's emotional response to it. For pain to be perceived by the individual, it must reach a conscious level.

Pain is initiated by a noxious stimulus, which may have one of three forms -- mechanical, chemical, or thermal -- at peripheral sites (Fishman & Carr, 1992; Guyton & Hall, 1996). The noxious stimulus causes depolarization of peripheral afferent nerve endings. If the depolarization is strong enough to generate an action potential, an impulse will travel along primary neurons from the periphery to the spinal cord. Secondary neurons originating in the spinal cord then transmit the impulse "to multiple brain sites where perceptive, evaluative, emotional, and cognitive responses to pain originate" (Puntillo & Tesler, 1993, p. 308). Activation of myelinated A-delta afferent fibers results in a sharp, fast, localized pain, whereas activation of unmyelinated C afferent fibers causes a more dull, slow, diffuse pain (Puntillo & Tesler, 1993; Guyton & Hall, 1996).

Kaul and Herring (1994) stated that pain from cooling is felt when tissue temperature is at or below 18°C (64.4°F). Findings from one study in which intramuscular

temperatures were measured suggested a relationship between intramuscular cooling and pain. Kregel, Seals, and Callister (1992) investigated the dynamics of temperature as a noxious stimulus affecting pain perception during localized skin cooling in ten healthy adults, eight men and two women. Before, during, and after a 3-minute immersion of one hand in water of different temperatures (28°, 21°, 14°, 7°, and 0°C) several physiological responses were measured. These included hand skin and esophageal temperatures which were measured by thermister probes and hand intramuscular temperatures which were measured by a thermocouple probe inserted at a depth of 1.5 centimeters into the interosseous muscle. Pain sensations were rated on a 15-point modified Borg scale. At 28° C and 21°C immersions, subjects had no sensation of pain. At 14°C, pain ranged from fairly mild discomfort to levels approaching painful. Measured hand skin temperature fell abruptly to approximately 23°C, then more gradually to approximately 19°C. Measured muscle temperature fell almost linearly from approximately 33 to 25°C. During the 7°C immersion, ratings of perceived pain approached painful and increased as skin temperature fell from approximately 17 to 14°C and muscle temperature fell to approximately 21°C. The entire 0°C immersion was perceived as intensely painful. Skin temperature fell to levels of 8 to 13°C and muscle temperature reached a final level of 18 to 21°C. During the 3-minute recovery period after the 0°C immersion, muscle temperature remained close to the end-immersion level, whereas skin temperature immediately rose toward the pre-immersion level. In addition, during the first 30 seconds of the recovery period, the intense sensation of pain persisted. In contrast, at the beginning of the recovery periods after the 28, 21, 14,and 7°C immersions, ratings of perceived pain decreased immediately. No studies have investigated the effect of cold as an internal noxious stimulus. This study compared cool and room temperature hepatitis B vaccine injected into muscle to examine the effect on adults' perception of pain intensity and unpleasantness.

Injection Pain and Management Strategies

Injection Pain

According to Eland (1981) and Fields (1987), injection pain results from two specific types of small fiber irritation. When the needle mechanically penetrates intact skin, cutaneous A-delta fibers are activated, causing a sharp, piercing "first pain," whereas a "second pain," a more dull and diffuse one, is caused by the activation of C fibers which are located in deep somatic structures such as ligaments, muscles, fascia, and joints (Puntillo & Tesler, 1993). Various techniques have been attempted to decrease injection pain and discomfort.

Strategies to Reduce Injection Pain

Site selection. Zelman (1961) recommended the upper outer quadrant of the buttock as the most advantageous site for intramuscular injection because it has a thick muscle that is free of major blood vessels and nerves. In comparison, the deltoid muscle is smaller and is supplied by many branches of the axillary nerve and humeral circumflex artery (Pitel & Wemett, 1964). According to Newton, Newton, and Fudin (1992), blood flow in the deltoid muscle is 7% greater than in the vastus lateralis and 17% greater than in the gluteal muscles. They suggest the use of the deltoid muscle for most small-volume and rapid-onset injections.

Injectate. Travell (1966) listed three causes of immediate pain of injection: local irritation, abnormal sensitivity of the tissue, and mechanical trauma. Mechanical trauma may arise from two mechanisms: penetration of the skin by the needle and sudden distention of tissue by the introduction of solution. In 1961, Zelman suggested that a slow rate of injection would allow more time for distention within the injected muscle and thereby decrease the pain sensation caused by activation of pressure-sensitive nerves within the muscle. Svendsen and Blom (1984) studied the effects of intramuscular injection volumes on injection sites in rabbits. They found that a small volume of a concentrated solution caused less muscle damage than a larger volume of a lesser

concentration. Injection speed was not found to be an important factor in local tissue reactions; fast and slow injections gave almost identical reactions. (Svendsen, 1984; Svendsen & Blom, 1984).

Brazeau and Fung (1989) studied damage in isolated rat muscle from injections with three mixed solvent systems: propylene glycol-water, ethanol-water, and polyethylene glycol 400-water. At moderate concentrations (20-40%, volume/volume) of the organic co-solvent, propylene glycerol was found to cause greater myotoxicity than ethanol and polyethylene glycol 400. The in vitro results were validated with in vivo studies on creatine kinase activity in rabbits after intramuscular injections. Svendsen and Blom (1984) reported that aqueous solutions of neuroleptic drugs caused greater local muscle damage than oily solutions. All aqueous preparations caused necrotic muscle tissue at the injection site, whereas no necrotic muscle tissue was found after the injection of haloperidol in sesame oil, methyl oleate, or squalane.

Muscle relaxation. Zelman (1961) found intramuscular injections in the dorsogluteal site to be less painful when the muscle was relaxed. Muscle relaxation was achieved with individuals in either a prone or a side-lying position and with the femur internally rotated by pointing the toes inward and the heels outward (Lang, Zawacki, & Johnson, 1976; Lang, Johnson, & Kruszewski, 1979; Retting & Southby, 1982; Zelman, 1961).

Locus of control. In a sample of 138 preoperative adults between the ages of 21 and 65, Levin (1982) found that neither having a choice of the vastus lateralis or ventrogluteal area for the preoperative injection nor locus of control affected the perception of pain. However, the study revealed that age, sex, and nurse variation had significant effects on the perception of pain. With increasing age, perceived pain following an intramuscular injection decreased. The youngest females experienced the greatest perception of pain after intramuscular injections. Of the two nurses who gave the injections, the one whose injections were rated as less painful worked in an acute care

setting, whereas the other nurse had some experience in an acute setting, but worked most recently in a mental health setting on a per diem basis.

Mechanical methods. Based on anecdotal experience, Wolf (1968) recommended a two-stage, controlled intramuscular injection technique to prevent painful local reactions and complications from intramuscular injections. In stage one, the needle was pushed through the skin and subcutaneous tissue at a 45° angle. In stage two, the needle and syringe were raised to a 90° angle with the needle tip resting on the surface of the muscle. The muscle was palpated beneath the needle and the syringe advanced further to penetrate the muscle.

Locsin (1985) tested a more practical pinch-grasp technique. In this technique, the deltoid muscle is grasped to elicit initial discomfort prior to the needle puncture of an intramuscular injection. Bourke (1985) found that scratching the skin 1 or 2 seconds before inserting a needle to inject local anesthetic solution and during the cutaneous infiltration reduced the discomfort of the injection. In 1986 and 1990, Keen found that the Z-track injection technique decreased the frequency of discomfort after injections as well as the frequency and severity of lesions at the injection sites and suggested that this technique be more widely used. Barnhill, Holbert, Jackson, and Erickson (in press) reported that a simple technique of applying manual pressure to the site prior to injection was useful in reducing injection pain

Topical applications. Taddio, Nulman, Goldbach, Ipp, and Koren (1994) found topical application of lidocaine-prilocaine 5% cream (eutectic mixture of local anesthetics, EMLA) to decrease injection pain in infants receiving diphtheria-pertussis-tetanus (DPT) vaccinations. Miser et al. (1994) reported that application of EMLA on skin decreased pain intensity scores of children undergoing central venous port implantation.

Cold applied to injuries has been used for centuries to decrease pain. Eland (1981) investigated the amount of injection site pain experienced by pre-kindergarten children after application of the skin coolant, Frigiderm spray, to the site immediately prior to the

injection of DPT vaccine. A sample of 20 girls and 20 boys was randomly assigned to one of four treatment groups: Frigiderm spray with cognitive information intended to alter the processing and interpretation of injection pain, Frigiderm spray without cognitive information, aerosol air spray with cognitive information, and aerosol air spray without cognitive information. The children who received Frigiderm spray reported significantly less pain than those who received the aerosol air spray, whereas cognitive information did not have a significant effect. The skin temperatures of the treatment groups were unreported.

Gedaly-Duff and Burns (1992) sought to replicate Eland's study. In pilot activities, they reported that the skin coolant caused a rebound burning sensation. They modified the independent variable to apply ice to the injection site 30 seconds before skin cleansing and the injection. Either DPT or diphtheria-tetanus (DT) vaccine was injected in an experimental group of 19 preschool children receiving ice compared to a control group of 19 preschool children who received no ice. The two groups did not differ significantly in pulse ratings or responses on the Global Mood Scale, Oucher scale, and Wong-Baker Faces scale.

Maikler (1991) studied the effects of a skin refrigerant/anesthetic on pain responses in infants receiving a routine DPT immunization. Of ten infant behaviors observed, only two, latency to cry and startle with needle insertion, reached statistical significance. Infants who were treated with the skin refrigerant/anesthetic startled less and began to cry later than those who did not have this treatment.

In 1986, Hillman and Jarman investigated the effect of ice as a local anesthetic agent. Sterile needles (Sabre type 25g Gillette) were attached to a De Fonbrune Micro-Manipulator and advanced one time at ten different sites on the left upper arm of each of the 20 adult subjects. The initial perceptions of touch and sharpness were noted for each of the ten needle advances. When the needle was advanced 2.66 mm (millimeters) from the surface of the skin or the subject felt the sharpness, the needle was withdrawn. Of 200

needle advances without use of ice, 190 were felt. Following the application of ice, however, only 89 of 200 needle advances were felt. Even though Hillman and Jarman, among others, suggest that ice has an anesthetic effect on the skin, Ernst and Fialka (1994) concluded that lack of rigorous research designs leaves the effectiveness of this method in question.

Summary

The review of literature indicates that various methods have been used to decrease injection pain and discomfort, including application of cold. Cold is known both to diminish and to instigate pain, depending on the temperature level. Cold applied as an analgesic prior to intramuscular injection of vaccines has been investigated in children, but not in adults. No studies have investigated the effect of the temperature of an injected solution as either an analgesic or a noxious stimulus. Therefore, this study was conducted to compare the effect of injected cool and room temperature hepatitis B vaccine on the perceived intensity and unpleasantness of injection pain in adults.

Hepatitis B Vaccine

Hepatitis B vaccine is a non-infectious recombinant DNA vaccine for intramuscular injection. In adults, the deltoid muscle is the preferred site for this injection since administration in the gluteal region results in lower immunogenicity (Merck Sharp & Dohme, 1995; SmithKline Beecham Pharmaceuticals, 1995; Atkinson, Furphy, Gantt, & Mayfield, 1995).

Van Damme, Cramm, Safary, Vandepapeliere, and Meheus (1992) investigated the heat stability of recombinant DNA hepatitis B vaccine in 138 healthy adults who were randomized to three groups. Group I received vaccine which had been stored for an unreported period at the recommended 4°C, Group II received vaccine which had been heated for one week at 45°C, and Group III received vaccine which had been heated for one month at 37°C. Subjects were asked to record on individual symptom sheets if they experienced soreness, induration, headache, fatigue, or fever on the day of vaccination and

for the following three days. The symptom sheet was not described nor was its reliability or validity mentioned. Soreness at the injection site was the most frequently reported local reaction (31.9%) for all injections and did not differ among the three groups. Fatigue (30.6%) and headache (25.8%) were the most common general reactions reported for all injections. Group II reported less headache (15.1%) and less fatigue (23.3%) compared to Group I (29.5%, 34.6%) and Group III (33.3%, 34.5%). Importantly, immunogenicity of the vaccine was not statistically different among the three storage temperatures.

Similar results were found by Just and Berger (1988) who studied 58 healthy young adults who were randomly assigned to receive hepatitis B vaccine that was either heated at 37°C for one week or stored at 4°C for an undetermined length of time. In both groups, soreness was the most common reported local reaction at the injection site. Other reported reactions including headache and fatigue. The data were collected after the subjects had completed a series of hepatitis B immunization. The investigators found no significant difference in reactogenicity and immunogenicity between the two solution temperatures.

The studies by Van Damme et al. (1992) and Just and Berger (1988) focused on long-term storage temperatures for the hepatitis B vaccine and did not identify the temperature of the vaccine as actually injected. Neither of the studies identified nor investigated the effect of cool and room temperature hepatitis B vaccine on the perceived pain intensity and unpleasantness at the time of injection.

Conceptual Framework

Pain intensity relates to the sensory-discriminative component of pain. It differs from the affective-motivational component of pain which has emotional properties and may be characterized as an unpleasantness experience (Johnson & Rice, 1974; Melzak & Wall, 1965, 1982). In addition, a cognitive-evaluative component of pain has been described (Melzack and Wall, 1965, 1982). These three components of pain guided Melzack and Wall in their development of the Gate Control Theory. This theory in

combination with currently known physiology was used as the conceptual framework for this study. Figure 1 shows a simplified description of pain transmission from the periphery to the brain.

The Gate Control Theory places emphasis on central transmission (T) cells in the dorsal horn of the spinal cord as the main gating site for pain modulation. Pain stimuli from the periphery are carried by small-diameter, myelinated A-delta afferent nerve fibers or unmyelinated C afferent nerve fibers to the dorsal horn. The T cells are believed to be excitatory fibers that are responsible for the central transmission of the pain stimuli from the spinal cord to the brain. Inhibitory interneurons in substantia gelatinosa of the dorsal horn are thought to influence the excitatory T cells by interacting with large-diameter, non-pain fibers and small-diameter pain fibers that synapse on the T cells. The inhibitory effect of these interneurons is reduced when the small-diameter pain fibers are activated, thus "opening" the pain gate and increasing transmission of pain signals by the T cells. In contrast, when the large-diameter, non-pain fibers are activated the inhibitory effect of these interneurons is increased, thus "closing" the pain gate and reducing transmission of pain signals by the T cells (Melzack & Wall, 1965, 1982). Pain impulses from the T cells are transmitted toward the brain via two major pathways: the neospinothalamic tract system and the paramedial ascending system. The neospinothalamic nerve fibers continue from the spinal cord into the ventrobasal thalamus and somatosensory cortex, whereas the fibers of the paramedial system continue into the reticular information, the medial and intralaminar thalamus, and the limbic system (Melzak & Wall, 1982). Modulation of sensory input through the neospinothalamic tract system provides a neurological basis for the sensory-discriminative component of pain, whereas activation of the limbic structures involves the affective-motivational component of pain (Guyton & Hall, 1996). The cognitive-evaluative component of pain is believed to be a combination of the sensory-discriminative component, the motivational-affective system, and higher central nervous system processes (Melzack & Wall, 1982).

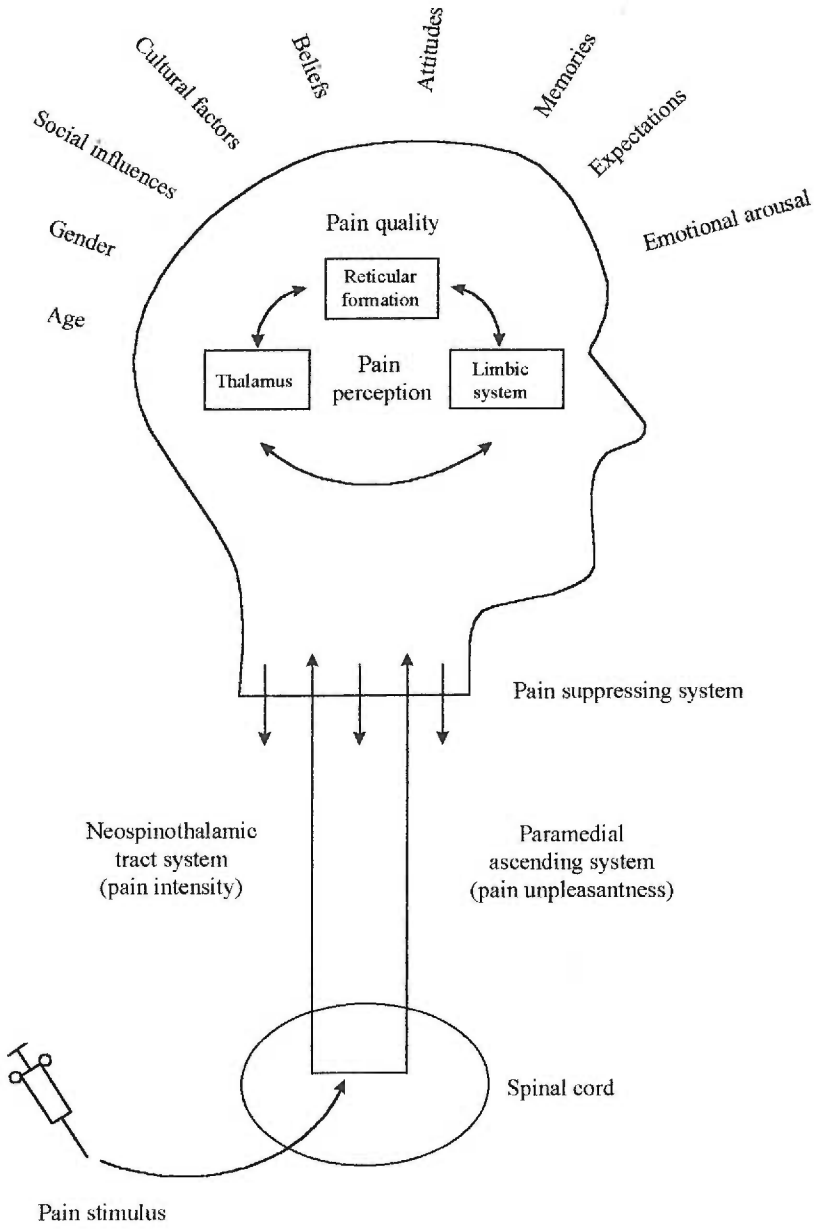

Figure 1. The intramuscular injection of hepatitis B vaccine as a noxious stimulus and its transmission to the brain via the two major pathways -- the neospinothalamic tract system and the paramedial ascending system -- and its transformation to a conscious level influenced by emotional arousal, expectations, memories, attitudes, beliefs, cultural factors, social influences, gender, and age.

The cerebral cortex may play an important role in interpreting the quality of pain whereas the conscious perception of pain may be related to lower central nervous system processes involving the limbic system, reticular formation, and thalamus (Guyton & Hall, 1996). According to the Gate Control Theory, higher central nervous system processes may deliver descending inhibitory messages to the spinal cord and decrease the pain experience (Puntillo & Tesler, 1993). In the lower central nervous system, such a neurological-based pain-suppressing system has been identified consisting of three major components: (a) the periaqueductal gray and periventricular areas of the mesencephalon and upper pons, (b) the raphe magnus nucleus located in the lower pons and upper medulla and the nucleus reticularis paragigantocellularis located laterally in the medulla, and (c) a pain inhibitory complex located in the dorsal horn of the spinal cord (Guyton & Hall, 1996). Factors without known physiological pathways that may influence lower and higher central nervous system processes with inhibitory and excitatory inputs include emotional arousal, expectations, memories, attitudes, beliefs, cultural factors, social influences, gender, and age (Chapman, 1980; Faucett, Gordon, & Levine, 1994; LeResche, 1995). For example, Fillingim and Maixner (1995) describe gender-associated differences in perceptual, emotional, and behavioral responses to noxious stimuli and state that neural mechanisms for these differences are beginning to be identified.

The peripheral pain stimulus in this study is the injection of hepatitis B vaccine into the deltoid muscle. Pain receptors are sparsely located in muscle and cause a dull, slow, diffuse pain when activated. Their activation can be elicited by chemical, mechanical, and thermal stimuli (Guyton & Hall, 1996). Injection involves all three stimuli. In this study, the focus is on thermal stimuli. For them to activate pain receptors, the temperature has to be extreme, either below 15°C (59°F) or above 45°C (113°F) (Guyton & Hall, 1996). Hypothetically, an injection of cool hepatitis B vaccine at approximately 9.4°C (49°F) may serve as a noxious stimulus, eliciting greater perception of pain and unpleasantness than an injection of hepatitis B vaccine at room temperature.

CHAPTER III

METHODS

Design

The study used an experimental design with subjects assigned to receive hepatitis B vaccine at one of two test temperatures. Group I received cool vaccine at approximately 9.4°C (49°F), while Group II received vaccine at room temperature of approximately 22.8°C (73°F). The effect of the two solution temperatures on experienced intensity and unpleasantness of injection pain was measured at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection.

Sample and Setting

Study subjects were a convenience sample of 64 individuals receiving hepatitis B vaccine injections over a 9-week data collection period. This sample size provided approximately an 80% chance, or power, of detecting a medium-sized effect for a two-tailed t-test at the 5% significance level (Cohen, 1988). The sample was obtained from three health clinics: the Employee Health Clinic at the Department of Veterans Affairs (VA) Medical Center, Portland, OR; the Employee Health Clinic at Oregon Health Sciences University (OHSU), Portland, OR; and the Health Services at Clark College, Vancouver, WA. (See Appendices A and B).

The secretaries in the three participating health clinics identified individuals scheduled for hepatitis B immunizations and inquired if they would speak to the investigator (see Appendix C). The investigator then explained the study to potential subjects and asked if they would participate. Subjects were at least 18 years of age, able to understand English, and able to rate intensity of pain and its unpleasantness. They had no known allergies to any of the components of the hepatitis B vaccine and had received fewer than five intramuscular injections in the past year. Subjects at the VA Employee Health Clinic signed a consent form (Appendix D), while those at the OHSU Employee Health Clinic and Clark College Health Services received a subject information form

(Appendix E). Pregnant women and breast feeding women were excluded, since it is unknown whether hepatitis B vaccine can cause fetal harm when administered to pregnant women or whether it is excreted in human milk (Merck Sharp & Dohme, 1995; SmithKline Beecham Pharmaceuticals, 1995). Subjects were randomly assigned to the two treatment groups. One die was thrown for each subject at each health clinic. If an even number showed, subjects received cool vaccine; if an odd number showed, they received room temperature vaccine. Subjects were blind to their group assignment.

Experimental Treatment

The independent variable was the temperature of hepatitis B vaccine at the time of injection. Group I received cool hepatitis B vaccine at approximately 9.4° (49°F) and group II received hepatitis B vaccine at room temperature of approximately 22.8°C (73° F). Subjects in both treatment groups received a 1-ml dose of vaccine containing 20 micrograms of hepatitis B surface antigen by intramuscular injection in either the left or right deltoid muscle, the recommended site (Merck Sharp & Dohme, 1995; SmithKline Beecham Pharmaceuticals, 1995). Subjects were asked to choose the side they preferred for the injection. Levin (1982) found that choice of site for preoperative injections among 138 preoperative adults did not affect their perception of injection pain. All injections in this study were administered by the investigator, and only vaccine manufactured by SmithKline Beecham Pharmaceuticals was used.

Prior to the study, the time required for hepatitis B vaccine to reach approximately 22.8°C (73°F) was determined by measuring the temperature of actual vaccine in three individual test vials. Immediately after each vial was removed from the refrigerator, an electronic pocket digital thermometer (TPD 31, Omega, Stamford, CT) was placed in the center of the vial. Every 15 seconds, the displayed temperature was recorded. The approximate time for a 1-ml volume of vaccine to rise from approximately 6.6°C (44°F) to approximately 22.8°C (73°F) was 21 minutes (Appendix F). Therefore, to obtain room temperature vaccine, each single dose vial was removed from the refrigerator a minimum

of 21 minutes prior to the injection. The vaccine was left in the vial until time of injection, then drawn into a 3-ml sterile syringe, using aseptic technique. At the OHSU Employee Health Clinic, two vials containing 0.5 ml vaccine were used. The vials were treated as a single dose vial and removed from the refrigerator a minimum of 21 minutes prior to administration. In comparison, in similar trials with 1 ml of 0.9% saline in three single dose 1-ml vials, the approximate time for the temperature to rise from approximately 6.6°C (44°F) to approximately 22.8°C (73°) was 13 minutes, 8 minutes less than required for the hepatitis B vaccine (Appendix F).

Prior to the study, the temperature of actual hepatitis B vaccine drawn up from three 1-ml vials into three separate 3-ml syringes immediately after removal from the refrigerator was determined (Appendix G). Before use, the syringes were stored in the refrigerator to minimize heat conduction to the cool vaccine. Immediately after the vaccine was drawn into the cool syringes, their plungers were removed and the electronic pocket digital thermometer was placed in the center of the syringes. The vaccine temperature reached 7.5-9.6°C (45.5-49.2°F) in 60 to 90 seconds (Appendix G).

Three trials were conducted to determine the length of time it would take the investigator to draw the hepatitis B vaccine into a syringe and administer the intramuscular injection (Appendix G). Approximately 70 to 80 seconds were needed when no interruptions interfered in the procedure, leaving the temperature of the injected vaccine at approximately 8.9°C (48°F). With a short interruption, such as answering a question, the necessary time to administer the injection was approximately 90 seconds, leaving the temperature of the injected vaccine at approximately 9.4°C (49°F). Typical room temperatures at the three study sites, measured by the electronic pocket digital thermometer, ranged from 21.9 to 23.4°C (71.5 to 74.2°F) with a mean of 22.8°C (73.1°F) (Appendix H).

The electronic pocket digital thermometer was tested against a certified reference thermometer (Taylor Scientific Instruments, Arden, NC) as the "gold standard" in a water

bath at two temperature ranges, 5 to 10°C (41 to 50°F) and 20 to 30°C (68 to 86°F). At the cool temperature range, the electronic pocket digital thermometer measured the temperature of the water bath to be 0.17 to 0.28°C (0.3 to 0.5°F) lower than the certified thermometer (see Figure 2). According to the technical specifications, the electronic pocket digital thermometer has a ± 1 percent full scale accuracy.

At the higher temperature range, the electronic pocket digital thermometer was tested against the "gold standard" thermometer in addition to two other reference thermometers, a certified (42261) and a precision-grade, but uncertified thermometer (32496) (Ever-Ready Thermometer Company, West Patterson, NJ). Between the temperatures of 20 to 24°C (68 to 75.2°F), the electronic pocket digital thermometer measured the temperature of the water bath to be 0.11 to 0.33°C (0.2 to 0.6°F) higher than the "gold standard" thermometer (see Figure 3). Between the temperatures of 25 to 30°C (77 to 86°F), the electronic pocket digital thermometer measured the temperature of the water bath to be 0.44 to 0.61°C (0.8 to 1.1°F) higher than the "gold standard" thermometer, 0.33 to 0.50°C (0.6 to 0.9°F) higher than reference thermometer 42261, and 0.33 to 0.61°C (0.6 to 1.1°F) higher than reference thermometer 32496. At these temperatures, the discrepancy between the water bath temperature, measured by the electronic pocket digital thermometer, and the three reference thermometers became greater (see Figure 3).

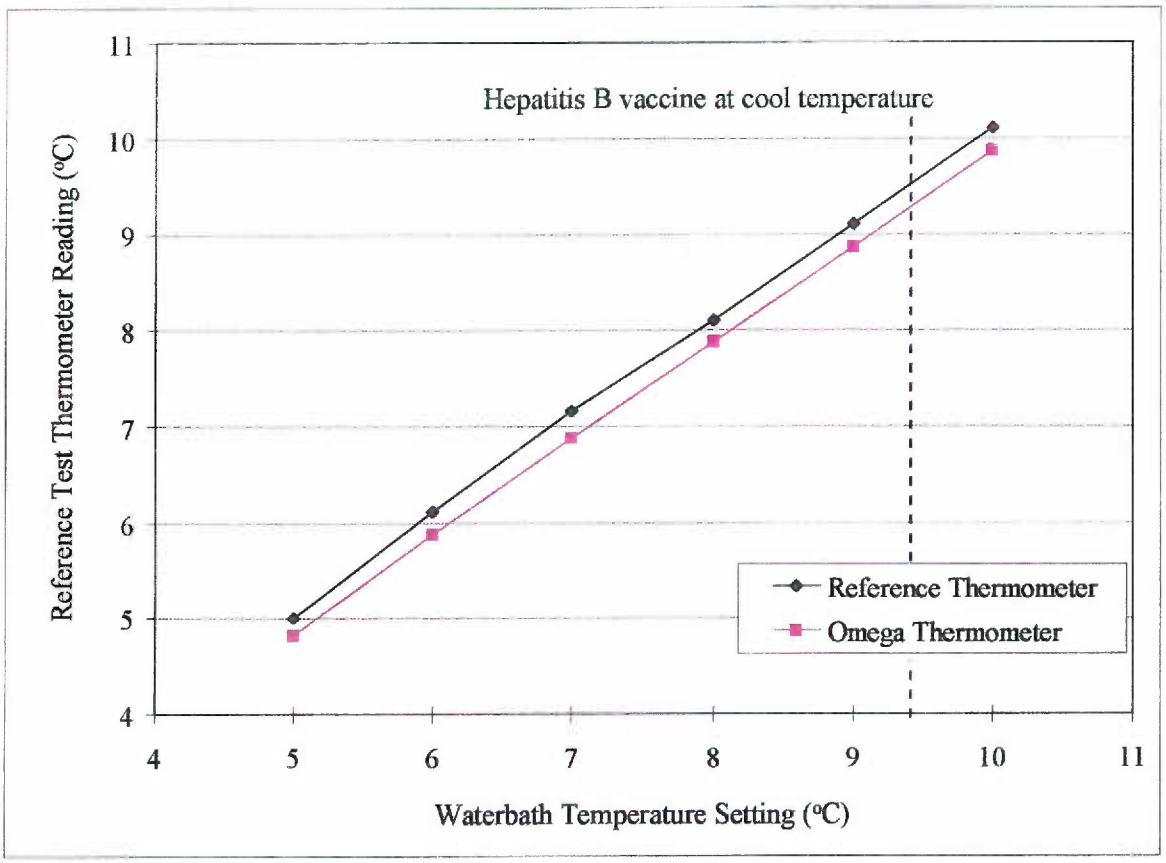

Figure 2. Cool temperature range.

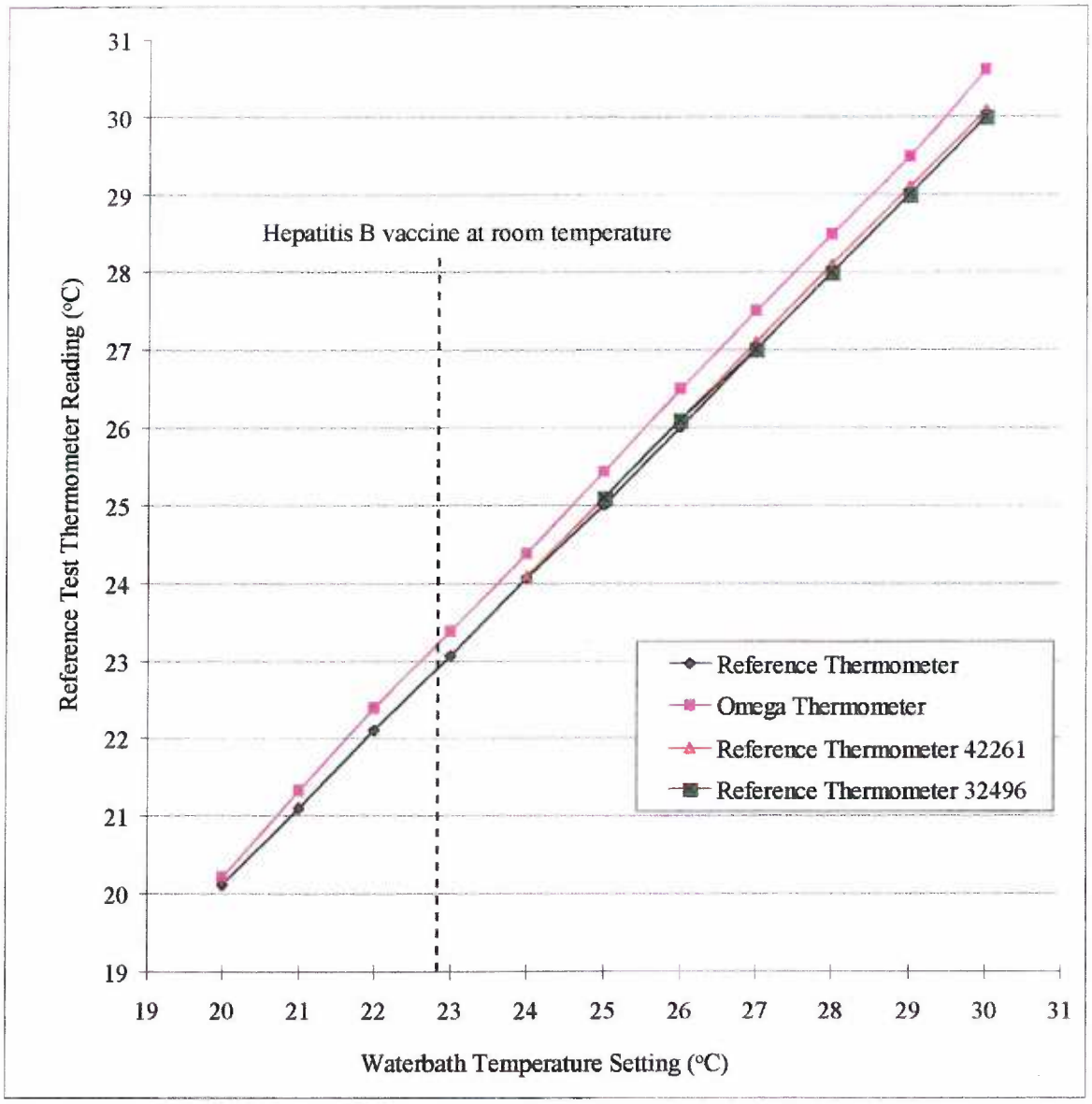

Figure 3. Warm temperature range.

Procedure

After subjects agreed to participate in the study, the investigator provided those at the VA Employee Health Clinic with a consent form to read and sign. At the OHSU Employee Health Clinic and Clark College Health Services, written consent was waived and subjects were provided with an information form. After the subjects finished reading the consent or information form, background data were obtained and written in the data collection booklet (Appendix I). Subjects were seen in an examination room to provide privacy and a quiet, comfortable environment.

For the injection, they were asked to sit on an examination table or a chair with the preferred arm slightly bent at the elbow and resting on the thigh to help relax the deltoid muscle. The recommended needle length for administrating hepatitis B vaccine at the deltoid site is 1 to 1½ inches in adults (Merck Sharp & Dohme, 1995). Which length of needle to use with each subject was determined by the pinch test (Lenz, 1983). On the opposite side from the injection site, the subcutaneous fat over the deltoid muscle was pinched slightly between the investigator's thumb and index finger. The approximate length of the needle required to reach into the deltoid muscle is about half the distance between the thumb and the index finger (Appendix J). To prevent tracking hepatitis B vaccine through the subcutaneous tissue, the needle used to draw up the vaccine was discarded and a new one attached to the syringe prior to the injection.

The injection site was wiped with 70% isopropyl alcohol which was allowed to dry while the investigator prepared the hepatitis B vaccine. The vial containing the vaccine was shaken gently to maintain suspension (Merck Sharp & Dohme, 1995; SmithKline Beecham, 1995). The vaccine dose to be administered was drawn up outside the examination room where the subject was waiting. This approach concealed whether cool or room temperature vaccine was administered. The vaccine was drawn into a sterile syringe using aseptic technique. The needle was inserted at a 90° angle into the body of the deltoid muscle, and aspiration was done to check for blood return. The vaccine was

then administered over approximately 5 seconds. After the needle was withdrawn, a dry cotton ball was placed over the site without pressure for 3-4 seconds. After removal of the cotton ball, the subject was asked by the investigator to rate the intensity and unpleasantness of injection pain (5 seconds) and a tape-recorded message cued them to do so 1, 5, and 10 minutes post-injection using visual analogue scales (VAS). The tape recorder was started after removal of the cotton ball, but before a small bandage was applied over the injection site. The investigator left the examination room while the subject completed the last three ratings to reduce the risk of bias. Several consumer magazines were available to subjects during the rating period. After 10 minutes, the investigator returned and thanked the subject for participating in the study. The data collection protocol is shown in Appendix K.

Measurement of Pain Intensity and Unpleasantness

The two dependent variables were subjects' ratings of the perceived intensity and unpleasantness of injection pain at 5 seconds, 1 minute, 5 minutes, and 10 minutes post injection using visual analog scales. To indicate the amount of pain they experienced, subjects were asked to make a vertical mark on a 100-mm horizontal line with anchors of "no pain" and "pain as bad as it could be." For the unpleasantness rating, the scale anchors were "no unpleasantness" and "unpleasantness as bad as it could be." Both scores were measured to the nearest 0.5 mm from the left end of the line.

The VAS was developed approximately 60 years ago to measure various subjective phenomena, but is most commonly used to measure the intensity of pain (McGuire, 1988). The VAS consists of a horizontal, or occasionally vertical, line 100 mm long with verbal descriptions of each extreme of pain intensity such as "no pain" to the "worst pain ever" or "pain as bad as it could be" (Carlsson, 1983; Downie et al., 1978; Kremer, Atkinson, & Ignelzi, 1981; Langley & Sheppeard, 1985; McGuire, 1988; Sriwatanakul et al., 1983). Subjects are asked to complete the scale by placing a vertical mark at the point that best represents their experienced intensity of pain at that particular

moment or at another designated time. Pain scores are calculated by measuring the distance in millimeters from the left end of the scale to the vertical mark, allowing quantification at the ratio level (Lee & Kieckhefer, 1989; Polit & Hungler, 1995).

Downie et al. (1978) compared the correlation between pain scores derived from the VAS and three other pain rating scales in studies of subjects with various rheumatic diseases. When the pain scales were presented to subjects in random order one after the other, the horizontal VAS was found to correlate well with the other scales ($r = .62$ to .92). When the time between completion of the pain scales was increased to 10 minutes, the correlation coefficients remained high ($r = .75$ to .91).

Price, McGrath, Rafii, and Buckingham (1983) investigated the intensity and unpleasantness dimensions of pain evoked by heat pulses in healthy subjects and subjects with chronic pain using VASs. They found the affective responses to pain to be more sensitive to contextual factors such as knowledge about the cause of pain than the sensory responses. Similar results were found by Price, Harkins, and Baker (1987) who studied subjects with labor pain and subjects with chronic pain. In both studies, the word "unpleasantness" was chosen as the verbal descriptor of the affective dimension of pain. The word "unpleasantness," as well as the word "intensity," may not necessarily have had the same meaning for each subject.

The VAS is very sensitive, as it provides an infinite number of responses between two extremes, allowing subjects to make as fine a discrimination as they wish (Lee & Kieckhefer, 1989). It is a simple, inexpensive measure of pain intensity and unpleasantness and can be completed in seconds, requires minimal energy, and is non-intrusive. Potential difficulties with the VAS include greater reproducibility at the extremes than at the midpoint, uninterpretable subject responses, and inaccurate measurement of the subject's mark on the line (Dixon & Bird, 1981; Huskisson, 1983; Herr & Mobily, 1993). Subjects with impaired motor skills, visual impairment, or a deficit in abstract thinking may have difficulty using the scale (Kremer et al. 1981; Lee & Kieckhefer, 1989). Kremer and

colleagues (1981) found older subjects less able to complete the VAS than younger ones. Herr and Mobily (1993) found their more educated subjects preferred the VAS when compared to their less educated subjects.

Protection of Human Subjects

This study proposal was reviewed by the Department of Veterans Affairs Medical Center Subcommittee on Human Studies, the Oregon Health Sciences University Committee on Human Research, and the clinic manager at each study site prior to commencement of data collection. At the VA Employee Health Clinic, subjects gave written informed consent before entry into the study. At the OHSU Employee Health Clinic and at Clark College Health Services, written consent was waived and subjects were provided with a subject information form. All subjects were free to withdraw from the study at any time. They received the hepatitis B vaccine injection regardless of their inclusion in the study. Confidentiality was protected by coding and reporting subject data by numbers.

The recommendation to store hepatitis B vaccine at 2 to 8°C (35°F to 46°F) raised the question of whether a brief period of warming it to room temperature would affect its immunogenicity. Two studies provided information about the effect of long-term periods of storing the vaccine at various temperatures. Van Damme et al. (1992) found that the geometric mean titer (GMT) of hepatitis B antibody (anti-HBs) was higher in the control group compared to the experimental groups after the third hepatitis B vaccine injection in a series of hepatitis B immunization. The control group received vaccines stored at 4°C. One experimental group received vaccines stored at 45°C for one week; the other experimental group received vaccines stored at 37°C for one month. The generally accepted protective GMT level of anti-HBs is 10 mIU/ml^{-1}. After one month, the GMT level was 65 mIU/ml^{-1} for the control group, 44 mIU/ml^{-1} for the experimental group which received vaccine stored at 45°C for one week, and 48 mIU/ml^{-1} for the experimental group which received vaccine stored at 37°C for one month. At 12 months, the levels of the

GMTs in all groups were between 1043 and 2018 mIU/ml^{-1}. The control group had the highest GMT level of 2018 mIU/ml^{-1}. Just and Berger (1988) found similar results. One month after the third hepatitis B injection, the GMT level was 2054 IU/L^{-1} in subjects who received vaccine stored at 4°C and 3392 IU/L^{-1} in those who received vaccine stored at 37°C for one week. However, no data suggest that a brief 21 minute period of warming one dose of hepatitis B vaccine to a room temperature of approximately 22.8°C (73°F), as used in this study, would affect the antibody level obtained.

Background Variables

Other variables which were accounted for included demographic variables of age, gender, marital status, ethnicity, educational level, and occupation, and injection variables of number of intramuscular injections in the past year, number of injection in the hepatitis B immunization series, and problems experienced with injections in the past. Variables that were not accounted for included subjects' emotional arousal, expectations, memories, attitudes, beliefs, and social influences that might affect their perception of pain (see Conceptual Framework, pp. 10-13).

Procedural variables which were controlled were the injection site, position of the subject's arm, type and volume of injected vaccine, skin preparation, needle length and gauge, aspiration time, length of time before the needle was withdrawn, and not massaging the skin after the injection. Subjects made the choice of receiving the injection in either left or right deltoid muscle. The investigator administered all injections.

Pilot Study

A pilot study was conducted with a convenience sample of twelve subjects, four men and eight women. Seven pilot subjects were obtained from the VA Employee Health Clinic, three from the OHSU Employee Health Clinic, and two from Clark College Health Services. All subjects received an intramuscular injection of hepatitis B vaccine administered by the investigator. The purpose of the pilot study was to evaluate possible pain measurement tools, the VAS to measure pain intensity in combination with either a

VAS or a 5-point verbal descriptor scale (VDS) to measure pain unpleasantness at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection. The scales were presented together on one page or on separate pages for each rating time so subjects would or would not be able to see their previous ratings. Each of the four combinations of the two scales were used and evaluated by three subjects (Appendix L).

Allowing subjects to see all their previous ratings might influence their responses as they would be able to compare the scores to one another. However, Scott and Huskisson (1979) found that subjects using a VAS overestimated their pain severity if previous scores were not available. In their study, the VAS was used as serial measurements of pain intensity in subjects receiving therapy from 2 weeks to 3 years. In this study, the serial measurements of pain intensity and unpleasantness were over a 10 minute period. None of the pilot subjects who had all their scores available on one page preferred to have had their scales listed on separate pages, and one of the six pilot subjects who used scales on separate pages would have preferred to have all scales available on one page. The VAS was chosen as the measurement tool for both pain intensity and unpleasantness ratings, with the scales for all four rating times presented on one page based on the possibility of comparing the two dependent variables, the short time period over which the ratings took place, and the convenience of listing all scales on one page. All VASs used were made by a computer and printed separately. Their length of 100 mm was measured and confirmed by the investigator.

Data Analysis

The two study groups were compared for equivalence in regard to background variables. Qualitative variables, including some demographic characteristics and past problems with injections, were compared using the chi square test. When the expected frequency in a cell fell below 5 in 2×2 comparisons, then Fisher's exact test was used (Daniel, 1995; Dawson-Saunders, 1994). Quantitative variables, including age, number of intramuscular injections received in the past year, and number of injection in the hepatitis

B immunization series, were compared using two-sample t-tests since the assumptions of normality, approximately equal variances, and independent samples were met (Daniel, 1995; Dawson-Saunders & Trapp, 1994). The study groups were compared in regard to pain intensity and unpleasantness using the Mann-Whitney U test, a nonparametric alternative to the t-test since these variables were not normally distributed. Most scores were concentrated at the lower end of the rating scales with some higher outlying values, resulting in peaked (leptokurtic) distributions with a positive skew. The .05 level of statistical significance was applied to all tests. Data analysis was done with the Crunch Statistical Package, Version 4 (Crunch Software Corporation, Oakland, CA).

CHAPTER IV

RESULTS

Characteristics of the Study Sample

A convenience sample of 64 subjects receiving hepatitis B vaccine injections was studied. Subjects ranged in age from 19 to 72 years, with a mean (± SD) age of 36.3 ± 12.9 years, and included 22 males and 42 females. Thirty-nine were employees or volunteers at the VA Employee Health Clinic, Portland, OR; 11 were employees at the OHSU Employee Health Clinic, Portland, OR; and 14 were students or employees at Clark College Health Services, Vancouver, WA. Data were collected over the 9 week period between February and April, 1996.

Thirty-three subjects were randomized to receive cool hepatitis B vaccine (Group I) and 31 to receive vaccine at room temperature (Group II). Tables 1 and 2 show the comparison of the two groups in regard to demographic variables and injection variables. No statistically significant differences were found for any of the background variables measured. Therefore, the groups were considered to be equivalent for the purpose of the study.

Pain Intensity and Unpleasantness

To compare the effect of the two temperatures of injected hepatitis B vaccine on pain intensity and unpleasantness, VAS scores at the four rating times in Groups I and II were compared with the Mann-Whitney U test. As shown in Table 3, subjects who received cool vaccine had a small, but statistically higher pain intensity rating at 5 seconds after the injection ($p = .01$). In this group, the median rating was 6.0 mm compared to 1.5 mm in the group that received vaccine at room temperature. The respective mean (± SD) ratings were 11.3 ± 13.3 mm and 5.1 ± 7.7 mm. At 1 and 5 minutes after the injection, the differences between the groups were close to or at statistical significance, but the numerical differences were so small as to be clinically unimportant. At 10 minutes, the

pain intensity ratings were negligible in both groups. At all four pain unpleasantness rating times, no statistical significance was found between the two study groups.

Table 1

Comparison of Demographic Variables in the Study Groups

Variable	Group I (cool vaccine) (n = 33)	Group II (room temperature vaccine) (n = 31)	Test statistic	p value
Age (yr)				
Median	36	32	$t = 0.68$	.50
Mean ± SD	37.4 ± 13.2	35.2 ± 12.7		
Range	19-72	21-69		
Gender				
Male	11	10	$\chi^2 = 0.01$	.93
Female	22	21		
Marital Status				
Single	12	11	$\chi^2 = 0.11$	.99
Married	17	16		
Divorced/widowed	4	4		
Ethnicity				
Caucasian	28	28	$\chi^2 = 0.44$	.51
Non-caucasian	5	3		
Education				
High school	5	2	$\chi^2 = 2.45$	.48
Some college	15	12		
College degree	7	11		
Postgraduate	6	6		
Occupation				
Health professional	11	10	$\chi^2 = 0.98$	.81
Health nonprofessional	4	2		
Other professional	6	8		
Other nonprofessional	12	11		
Study site				
Clark college	8	6	$\chi^2 = 0.34$	.84
VA Medical Center	19	20		
OHSU	6	5		

Table 2

Comparison of Injection Variables in the Study Groups

Variable	Group I (cool vaccine) (n = 33)	Group II (room temperature vaccine) (n = 31)	Test statistic	p value
Number of IM injections in the past year				
Median	1	2	t = -1.07	.23
Mean ± SD	1.4 + 1.1	1.6 ± 1.0		
Range	0-4	0-4		
Injection number in hepatitis B series				
Median	2	2	t = -1.11	.27
Mean ± SD	2.0 ± 1.1	2.3 ± 1.0		
Range	1-5	1-4		
Problems with IM injections in the past year				
Yes	9	7	$\chi^2 = 0.19$	.66
No	24	24		
Tenderness	8	6	--	--
Redness	1	1	--	--
Swelling	4	0	--	--
Bruising	4	1	--	--
Injection site				
Left deltoid	32	29	Fisher's	.61
Right deltoid	1	2		
Needle length				
1"	32	31	Fisher's	1.00
1 ½"	1	0		

Note. IM = intramuscular injection; SD = standard deviation; t = two-sample t-test; χ^2 = chi-square test; Fisher's = Fisher's exact test.

Table 3

Comparison of Reported Pain Intensity and Unpleasantness in the Study Groups

Variable	Group I (cool vaccine)	Group II (room temperature vaccine)	Mann - Whitney z score	p value
		Pain intensity score		
5 seconds				
Median	6.0	1.5	2.69	.01[α]
Mean ± SD	11.3 ± 13.3	5.1 ± 7.7		
Range	0-55.5	0-35.0		
1 minute				
Median	2.0	0.0	1.91	.06
Mean ± SD	5.7 ± 10.8	2.4 ± 3.9		
Range	0-58.5	0-14.5		
5 minutes				
Median	0.5	0.0	2.89	<.01[α]
Mean ± SD	2.2 ± 7.8	1.0 ± 3.5		
Range	0-45.0	0-18.0		
10 minutes				
Median	0.0	0.0	1.52	.13
Mean ± SD	1.0 ± 3.5	0.6 ± 1.6		
Range	0-20.0	0-7.0		
		Pain unpleasantness score		
5 seconds				
Median	2.5	1.0	1.86	.06
Mean ± SD	6.2 ± 8.9	4.1 ± 9.4		
Range	0-33.5	0-49.5		
1 minute				
Median	1.0	0.0	1.58	.12
Mean ± SD	3.4 ± 5.2	1.5 ± 2.2		
Range	0-19.0	0-7.0		
5 minutes				
Median	0.5	0.0	1.17	.24
Mean ± SD	1.0 ± 1.8	1.9 ± 6.4		
Range	0-8.0	0-35.5		
10 minutes				
Median	0.0	0.0	1.15	.25
Mean ± SD	0.7 ± 1.8	0.6 ± 1.7		
Range	0-9.5	0-8.0		

Note. SD = standard deviation.

α with correction for the four multiple comparisons of pain intensity, $p < .05$.

The relative low median and mean values of pain intensity in the grouped data may obscure the more important finding that in some subjects, pain intensity ratings moved more markedly from mild toward moderate levels when cool vaccine was administered. The median difference of 4.5 mm in pain intensity ratings at 5 seconds was relative small. However, of the seven subjects with individual ratings over 20 mm at 5 seconds, six had received cool vaccine and only one had received vaccine at room temperature (Table 4, Figures 4 and 5). In addition, six of the seven subjects with ratings above 20 mm were women and six were below the mean age of 36 years; five of them women. Only one subject, a 23-year old nonprofessional female, reported pain intensity ratings at or above 20 mm at all four ratings.

Of the four subjects with individual pain unpleasantness ratings above 20 mm at 5 seconds, three had received cool vaccine and only one had received vaccine at room temperature (Figures 6 and 7). The subjects were all women and three of them were below the mean age of 36 years. Two of them were health professionals, one was a health nonprofessional, and one was a non health professional.

Table 4

Number of Pain Ratings Above and Below 20 mm

Pain intensity rating at 5 seconds	Group I (cool vaccine) (n = 33)	Group II (room temperature vaccine) (n = 31)
≤ 20 mm	27 (82%)	30 (97%)
> 20 mm	6 (18%)	1 (3%)

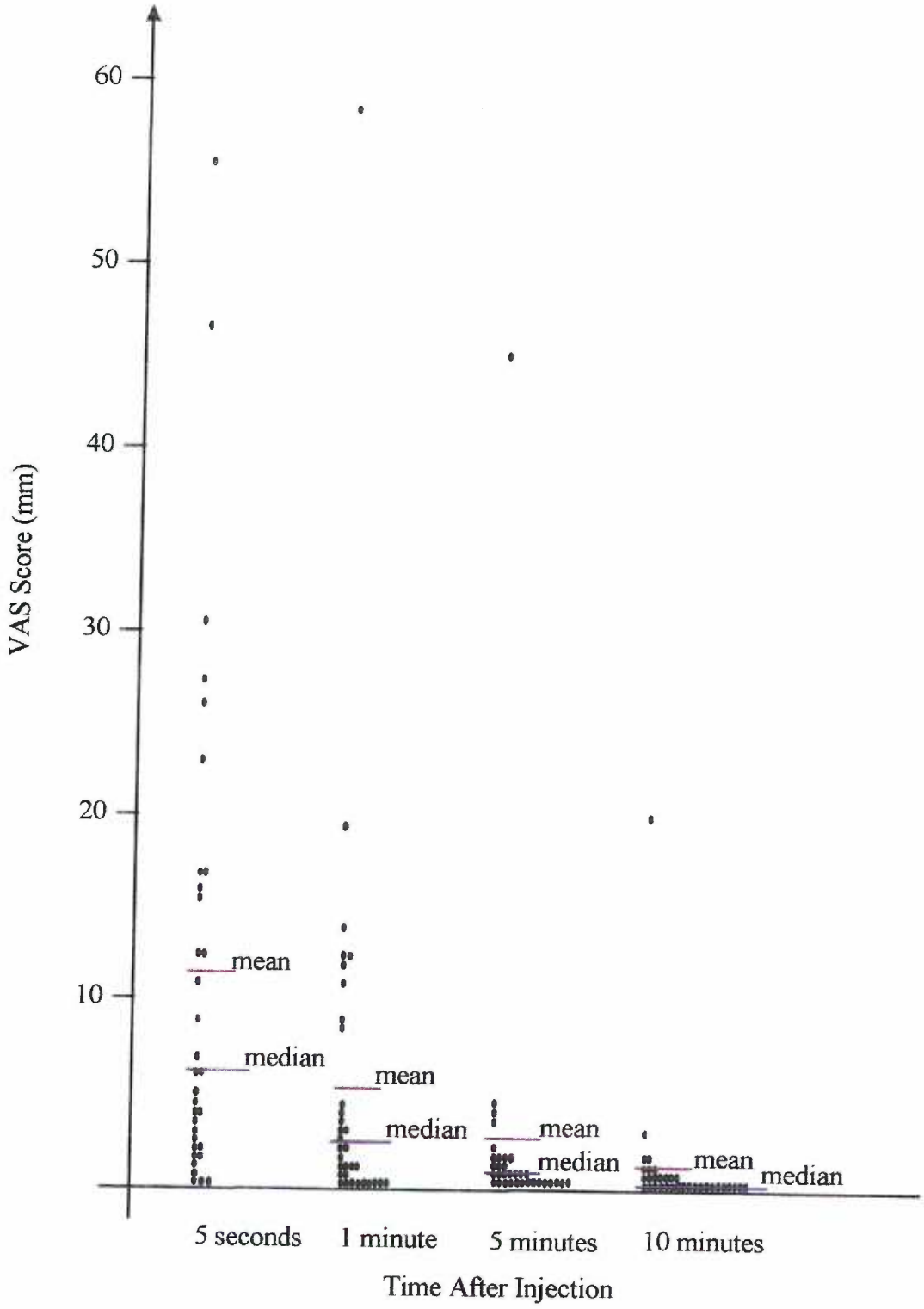

Figure 4. Individual pain intensity ratings in Group I (cool vaccine).

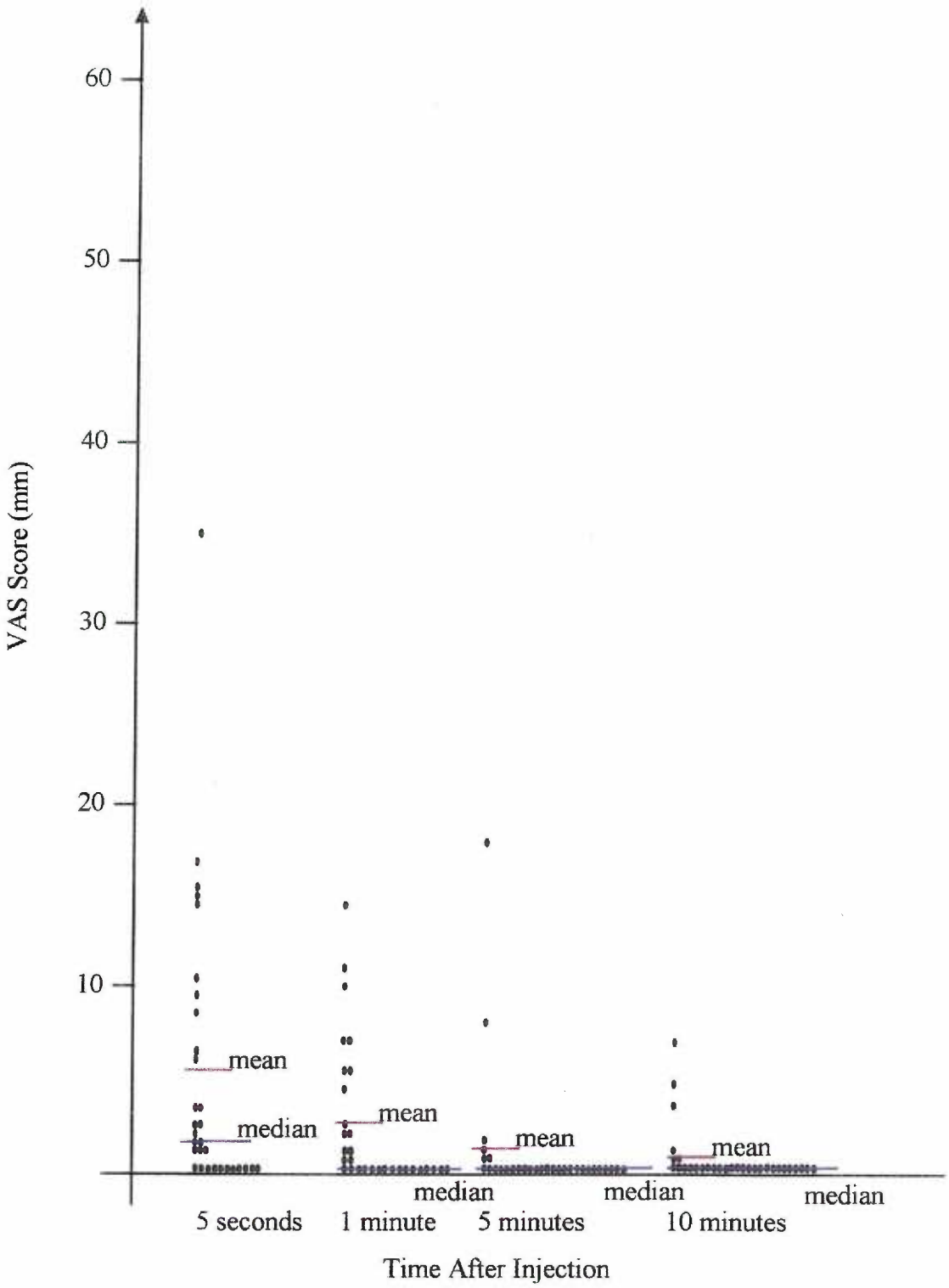

Figure 5. Individual pain intensity ratings in Group II (room temperature vaccine).

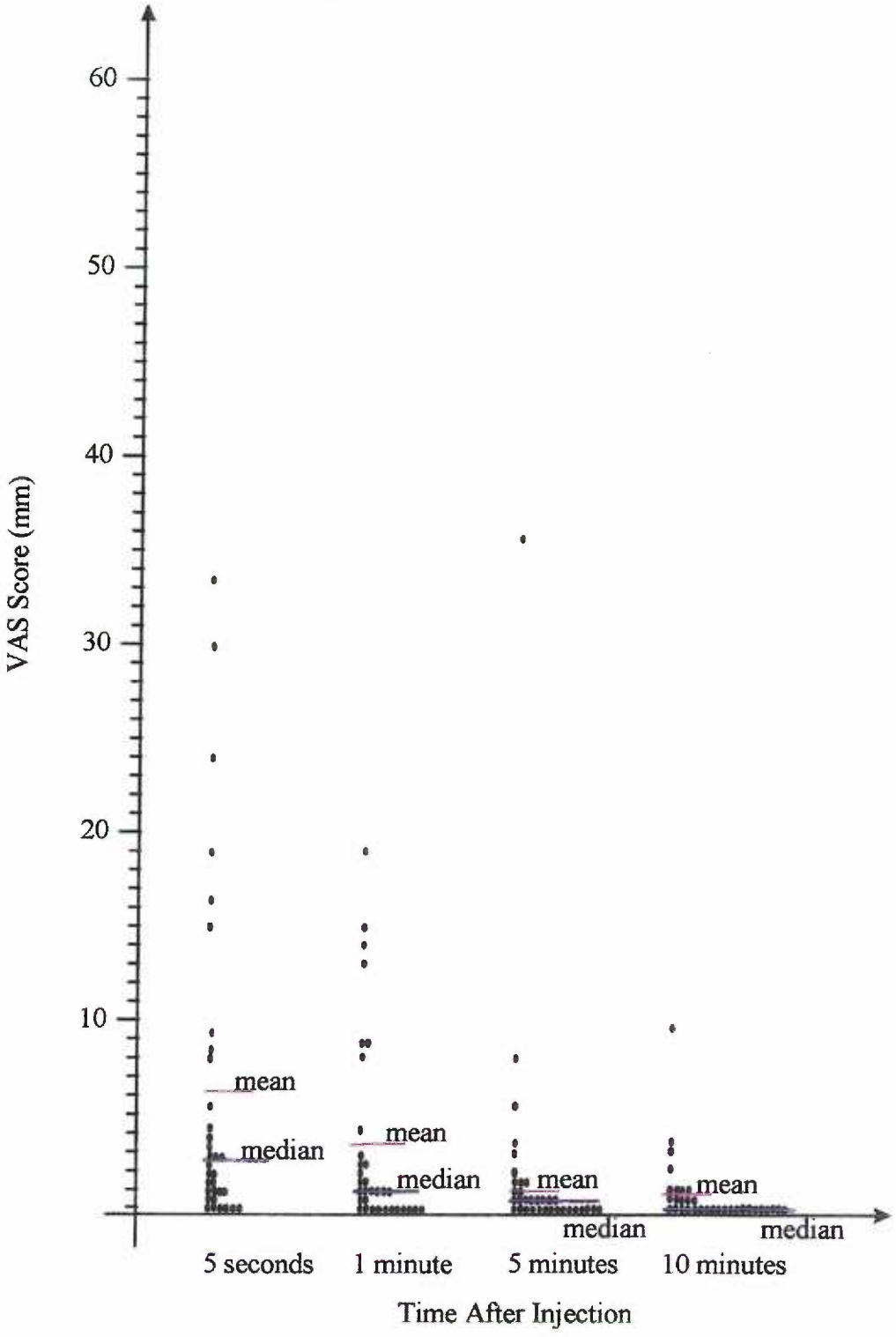

Figure 6. Individual pain unpleasantness ratings in Group I (cool vaccine).

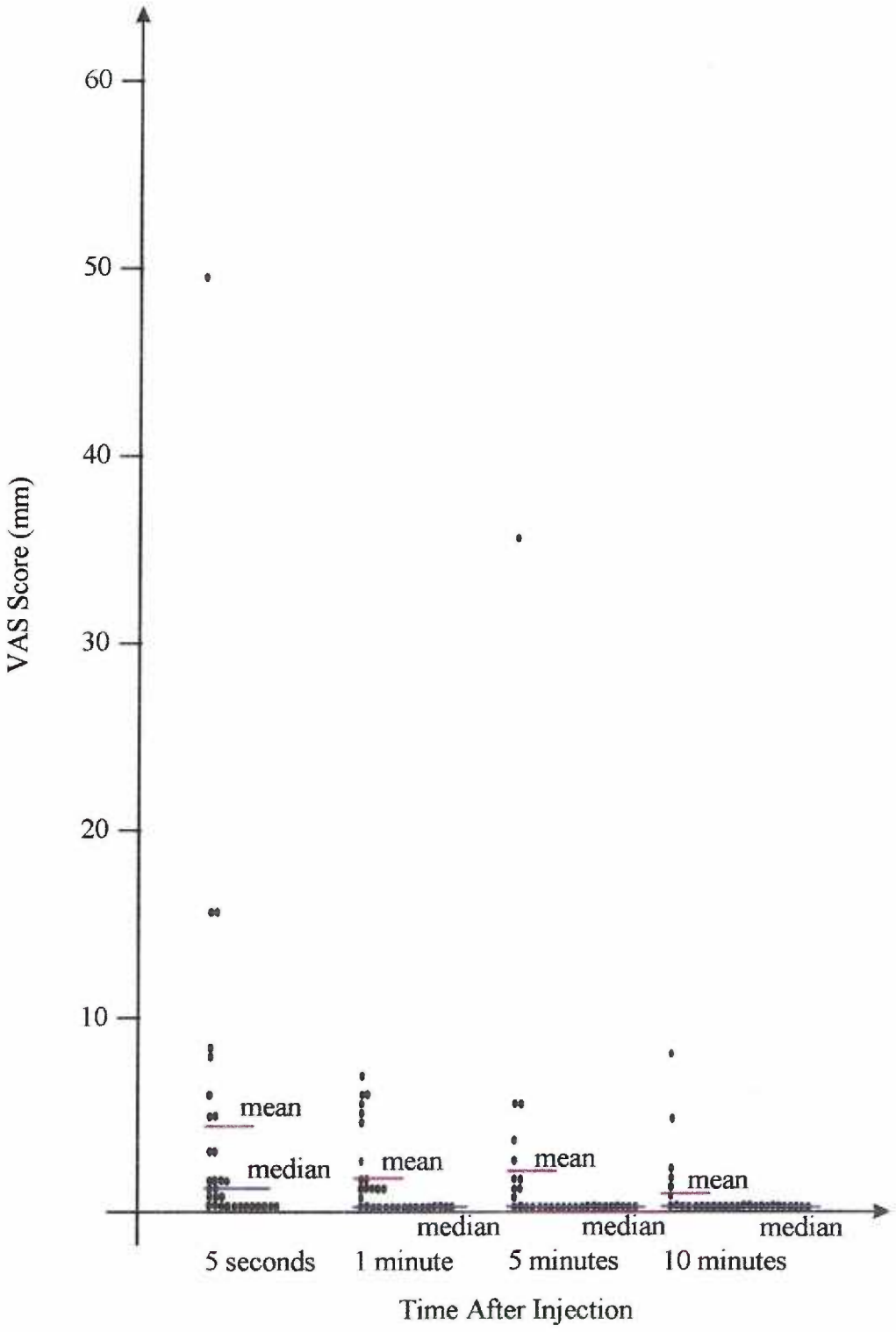

Figure 7. Individual pain unpleasantness ratings in Group II (room temperature vaccine).

CHAPTER V

DISCUSSION

The purpose of this study was to compare the effect of the two temperatures of injected hepatitis B vaccine, cool (approximately 9.4°C [49°F]) and room temperature (approximately 22.8°C [73°F]), on perceived pain intensity and unpleasantness at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection. The difference between the 33 subjects who received cool vaccine (Group I) and the 31 subjects who received vaccine at room temperature (Group II) was statistically significant at 5 seconds after the injection. In Group I, the median rating was 6.0 mm and in Group II 1.5 mm. The respective mean ratings were 11.3 and 5.1 mm. The relative low ratings experienced with intramuscular injections in this study were consistent with the magnitude of the noxious stimulus. Injection involves three kind of noxious stimuli: chemical, mechanical, and thermal. In this study, the focus was on thermal stimuli. Barnhill et al. (in press) found that applying pressure for 10 seconds to the injection site prior to an intramuscular injection reduced injection pain. In their study involving intramuscular administration of gamma globulin at the dorsogluteal site, the median VAS rating of pain intensity was 9.0 mm when pressure was applied and 16.0 mm when it was not; the respective mean ratings were 13.6 and 21.5 mm. In the present study, intramuscular injection pain intensity and unpleasantness ratings were reported as mild for most subjects, but seven subjects had individual pain intensity ratings above 20 mm and four subjects had individual pain unpleasantness ratings above 20 mm immediately after the injection. In contrast, Duggleby and Lander (1994) found that mean pain intensity and unpleasantness ratings during the first 14 hours after total hip replacement ranged between 20 and 60 mm. In addition to

being a generally mild noxious stimulus, the hepatitis B vaccine injection may be perceived as a beneficial protection toward the disease and therefore not perceived as being a great noxious stimulus or threat. Price and colleagues (1987) found patients in labor and patients exposed to experimental pain to have lower VAS unpleasantness ratings compared to their intensity ratings of pain. Furthermore, they found VAS unpleasantness ratings to be higher in cancer pain patients and chronic pain patients compared to their VAS intensity ratings of their clinical pain. If there is no threat to health or life, which is the case with brief experimental pain, or if pain has a positive outcome, as is most often the case with patients in labor, they suggest that the affective dimension of pain can be selectively influenced by the individual.

The conceptual framework for this study is in agreement with the study findings in that an injection of cool hepatitis B vaccine provided a greater noxious stimulus of pain intensity than an injection of hepatitis B vaccine at room temperature. However, an injection of cool hepatitis B vaccine provided no greater noxious stimulus of pain unpleasantness compared to an injection of hepatitis B vaccine at room temperature, perhaps due to the relative unthreatening nature of the immunization..

At the deltoid site the injection of hepatitis B vaccine served as a noxious stimulus causing pain impulses to be transmitted via the neospinothalamic tract and paramedial ascending system to the brain where impulse transformation into awareness may have been influenced by factors not accounted for such as emotional arousal, expectations, memories, attitudes, beliefs, cultural factors, and social influences. Age and gender, which were accounted for, are of interest because six of the seven subjects reporting pain intensity above 20 mm were women, and six of the seven were younger than the mean age

of 36 years. Of these six, five were women. Similar findings were described by Faucett and colleagues (1994) in a study on acute postoperative dental pain; in 543 subjects 242 were men and 301 women. According to Fillingim and Maixner (1995), women may be more sensitive to noxious stimuli than men. They reported that women have been found to be more sensitive to pain in laboratory studies using mechanical pressure, whereas results from laboratory studies using thermal pain have been inconclusive. The authors proposed a model of how biological and psychological factors may contribute to gender differences in pain experiences. They described how pain responses may vary along several dimensions, including sensory, affective, cognitive-evaluative, physiological, and behavioral. In this clinical study, the sensory-discriminatory and affective-evaluative components of pain were measured, whereas the cognitive-evaluative component which relates to cognitive strategies as well as expectations and beliefs concerning pain was not.

Harkins, Price, and Martelli (1986) investigated the effect of age on pain perception in 44 adults. They divided the subjects into three groups consisting of young (age range 20 to 36 years), middle-aged (age range 45 to 60 years), and elderly (age range 65 to 80 years). All subjects received noxious heat stimuli delivered to the forearm of their non-dominant arm at 6 intensities (43°, 45°, 47°, 48°, 49°, and 51°C). Each noxious stimuli lasted 5 seconds. Findings indicated that older adults have a tendency to underrate low and overrate higher pain intensity caused by contact heat when compared to ratings by younger adults. A similar result was described by Levin (1982) in his study of 138 adults between the ages of 21 and 65 who received intramuscular preoperative injections. With increasing age, the post injection pain decreased. Furthermore, the younger the women, the higher the intensity of the reported pain.

The VAS as a Measurement Tool

Although educational level and age have been reported as factors in subjects' abilities to complete the VAS (Kremer et al., 1981; Herr & Mobily, 1993), none of the subjects in this study seemed to have difficulty rating their experienced pain intensity and unpleasantness by placing a vertical mark on the horizontal 100 mm lines. None were excluded due to incorrect marking on the lines. The sensitivity of the VAS allowed for discrimination between the ratings at the relative low levels predominantly found in the study.

Limitations of the Study

Several limitations were noted in the study. First, the exact temperature of the cool injected hepatitis B vaccine was unknown. Due to questions asked by some subjects prior to receiving the vaccine, the injection may have been delayed for a few seconds, extending the estimated time for the injection beyond 90 seconds. Although the approximate temperatures of the refrigerators at the three study sites were known (Appendix H), periods of time when the refrigerator doors were opened because of many immunizations being given may have resulted in higher than measured refrigerator temperatures. However, it was unlikely that the cool vaccine used in this study exceeded a temperature of 15°C (59°F), the level of cold stimulus known to activate pain receptors. A time of approximately 4 minutes and 45 seconds would be required for the hepatitis B vaccine to reach this level, far longer than required for the injection procedure.

The second limitation is that the exact rating times at 1 minute, 5 minutes, and 10 minutes are unknown. The investigator left the examination room while the subject

completed the last three ratings. Whether the subject followed the instructions as indicated by the tape-recorded message was not determined.

The third limitation is the homogenity of the sample and injectate used. Only subjects who received hepatitis B vaccine participated in the study. They were mainly Caucasians. Other types of injected solutions may cause different levels of pain. In addition, according to Faucett et al. (1994) and Bates, Edward, and Anderson (1993), pain severity may vary in different ethnic and cultural groups.

The fourth limitation may be related to response bias or perhaps subjects' inability to feel or discriminate between pain intensity and unpleasantness. Ten of the 33 subjects in Group I and 19 of the 31 subjects in Group II had pain intensity and unpleasantness scores within 2 mm of one another at all rating times. Nine subjects (three men and six women) had perfect scores with no reported pain intensity and unpleasantness. Whether their lower and higher central nervous system processes were blocked from the noxious is unknown. One man and one woman reported no pain intensity, but did experience pain unpleasantness. These findings are not consistent with the model of affective-motivational dimension of pain proposed by Price and Harkins (1992). They question whether affective-motivational and sensory-discriminative dimensions of pain are processed in parallel or consecutively. As discussed earlier, they suggest that pain affective responses are the result of several contributing factors, but mostly by the painful sensation it self. Whether gender differences exist in discriminating noxious stimuli which include studies of thermal pain remains to be determined (Fillingim & Maixner, 1995).

The fifth limitation may have been investigator bias. All hepatitis B vaccine injections were administered by the investigator who was aware of each individual

subject's group assignment. This information was necessary for the investigator to conduct the study, but may have contributed to bias.

Future Practice and Research

A replication study is needed to confirm the tendency of hepatitis B vaccine at room temperature to cause less discomfort than cool hepatitis B vaccine the first 5 minutes post injection. It is not known whether the low scores at 1 minute after the injection may be due to distraction of the subjects, i.e., by interactions such as the subjects picking up reading material or getting dressed. Further research is needed in other populations and with other vaccines typically stored in refrigerators. A population of particular interest may be children, since fear of pain may make injections difficult for them. Expansions on this study could be the investigation of other rating times post injection, e.g., 30 seconds, 1 minute and 30 seconds, 2 minutes, and 3 minutes to better describe the pain experienced by subjects early on. Whether warming hepatitis B vaccine to room temperature influences its immunogenicity could be investigated by obtaining antibody levels of all subjects.

Most healthy adults receiving an intramuscular hepatitis B vaccine injection report minimal discomfort, but this study suggests that as many as one in five may experience moderate levels of pain at least initially after the injection. Reducing injection discomfort for these individuals by administering hepatitis B vaccine at room temperature would be beneficial, and requires little clinical effort.

Findings from this study support that an injection of cool hepatitis B vaccine of approximately 9.4°C (49°F) initially served as a stronger noxious stimulus, eliciting a higher pain intensity than an injection of hepatitis B vaccine at room temperature. This

suggests that warming the vaccine to room temperature provides a simple strategy to reduce the initial pain of routine hepatitis B immunizations.

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APPENDIX A

LETTERS SENT

OREGON
HEALTH SCIENCES UNIVERSITY
3181 S.W. Sam Jackson Park Road, Portland, OR 97201-3098
Mail Code SN-AHI, (503) 494-7839

School of Nursing
Department of Adult Health and Illness

Tiffany Simons, ANP
VA Employee Health
P. O. Box 1034
Portland, OR 97207

December 27, 1995

Dear Tiffany Simons,

As a graduate student at the School of Nursing of the Oregon Health Sciences University, part of my program includes conducting a master's research project. I am planning to investigate the effect of hepatitis B vaccine temperature on injection pain. One group of people will receive cool vaccine at approximately 46°F. The second group will receive vaccine at room temperature of approximately 74°F. Following the injection, the participants will be asked to rate their perceived intensity of injection pain on a visual analogue scale and the unpleasantness of the pain on a verbal descriptor scale.

I would like to conduct the study with employees attending Employee Health at the Department of Veterans Affairs Medical Center. The study will be explained to each potential participant, written informed consent obtained, and demographic data collected. The names or identity of the participants will not be used as the study records will be identified by code numbers. The study participants will be a convenience sample of approximately 65 individuals receiving hepatitis B vaccine injections at three different study settings including Employee Health, Oregon Health Sciences University, Portland and Health Services, Clark College, Vancouver.

Prior to the time of data collection, a copy of the data collection protocol will be made available. I appreciate your time and consideration of this study. Please let me know if I will be able to conduct a part of this study at the Employee Health and if so confirm that the Employee Health will treat any complications the participants may experience as a result of the hepatitis B vaccine.

Sincerely,

Lissi Hansen

Lissi Hansen

P. S. Please address further correspondence to the following address: Lissi Hansen
15708 SE Evergreen Hwy
Vancouver, WA 98684

cc: Debbie Burton
Mary B. Maxwell

OREGON
HEALTH SCIENCES UNIVERSITY
3181 S.W. Sam Jackson Park Road, Portland, OR 97201-3098
Mail Code SN-AHI, (503) 494-7839

School of Nursing
Department of Adult Health and Illness

Nina Wolf, RN
Nurse Manager
OHSU Employee Health

December 27, 1995

Dear Nina Wolf,

As a graduate student at the School of Nursing of the Oregon Health Sciences University, part of my program includes conducting a master's research project. I am planning to investigate the effect of hepatitis B vaccine temperature on injection pain. One group of people will receive cool vaccine at approximately 46°F. The second group will receive vaccine at room temperature of approximately 74°F. Following the injection, the participants will be asked to rate their perceived intensity of injection pain on a visual analogue scale and the unpleasantness of the pain on a verbal descriptor scale.

I would like to conduct the study with employees attending Employee Health at Oregon Health Sciences University. The study will be explained to each potential participant who will be given a participant information form. The study data and demographic data will be collected in a data collection form booklet. The names or identity of the participants will not be used as the study records will be identified by code numbers. The study participants will be a convenience sample of approximately 65 individuals receiving hepatitis B vaccine injections at three different study settings including Employee Health, Department of Veterans Affair Medical Center, Portland and Health Services, Clark College, Vancouver.

Enclosed is a copy of the participant information form. Prior to the time of data collection, a copy of the data collection protocol will be made available. I appreciate your time and consideration of this study. Please let me know if I will be able to conduct a part of this study at the Employee Health and if so confirm that the Employee Health will treat any complications the participants may experience as a result of the hepatitis B vaccine.

Sincerely,

Lissi Hansen

Lissi Hansen

P. S. Please address further correspondence to the following address: Lissi Hansen
15708 SE Evergreen Hwy
Vancouver, WA 98684

OREGON
HEALTH SCIENCES UNIVERSITY
3181 S.W. Sam Jackson Park Road, Portland, OR 97201-3098
Mail Code SN-AHI, (503) 494-7839

School of Nursing
Department of Adult Health and Illness

Mary Deal
Director of Health Services
Clark College
1800 E. McLoughlin Blvd.
Vancouver, WA 98663

December 27, 1995

Dear Mary Deal,

As a graduate student at the School of Nursing of the Oregon Health Sciences University, part of my program includes conducting a master's research project. I am planning to investigate the effect of hepatitis B vaccine temperature on injection pain. One group of people will receive cool vaccine at approximately 46°F. The second group will receive vaccine at room temperature of approximately 74°F. Following the injection, the participants will be asked to rate their perceived intensity of injection pain on a visual analogue scale and the unpleasantness of the pain on a verbal descriptor scale.

I would like to conduct the study with college students 18 years or older attending Health Services at Clark College. The study will be explained to each potential participant who will be given a participant information form. The study data and demographic data will be collected in a data collection form booklet. The names or identity of the participants will not be used as the study records will be identified by code numbers. The study participants will be a convenience sample of approximately 65 individuals receiving hepatitis B vaccine injections at three different study settings including Employee Health, Department of Veterans Affairs Medical Center, Portland and Employee Health, Oregon Health Sciences University, Portland.

Enclosed is a copy of the participant information form. Prior to the time of data collection, a copy of the data collection protocol will be made available. I appreciate your time and consideration of this study. Please let me know if I will be able to conduct a part of this study at the Health Services and if so confirm that the Health Services will treat any complications the participants may experience as a result of the hepatitis B vaccine.

Sincerely,

Lissi Hansen

Lissi Hansen

P. S. Please address further correspondence to the following address: Lissi Hansen
15708 SE Evergreen Hwy
Vancouver, WA 98684

cc: Tana Hasart

APPENDIX B

LETTERS RECEIVED

DEPARTMENT OF VETERANS AFFAIRS
Medical Center
3710 Southwest U.S. Veterans Hospital Road
Portland OR 97201

In Reply Refer To:

Lissi Hansen
15708 SE Evergreen Hwy
Vancouver, WA 98684

December 28, 1995

Ms. Hansen,

This letter is in response to your correspondence requesting cooperation with your upcoming research study investigating the effects of Hepatitis B vaccine temperature in relation to perceived pain at injection site. Employee Health is happy to assist you in this study and we will schedule as many injections as possible on monday afternoons throughout the course of your project.

The Employee Health Nurse Practitioner will be on site while injections are being provided to treat any complications the participants may experience as a result of the hepatitis B vaccine. The employees receiving the vaccine are doing so voluntarily and will have a consent on file prior to the administration of the vaccine.

Please forward a copy of your proposal and participation consent prior to January 22, 1996. I look forward to assisting you in this research study.

Tiffany Simons, ANP

Tiffany Simons RN, MS, ANP
Employee Health Nurse Practitioner

MEMORANDUM

THE OREGON HEALTH SCIENCES UNIVERSITY

Employee Health
(503) 494-5271
Fax # (503) 494-2746

DATE: December 27, 1995

TO: Lissi Hansen, RN

FROM: Nina Wolf, RN, COHN

SUBJECT: Master's research project

Employee Health will be pleased to assist you in any way reasonable in collecting data for your research study. We will, in fact, be responsible for treating any complications the participants may experience as a result of the hepatitis B vaccine, just as we would if the vaccine were administered by Employee Health independent of your study.

Please let me know if there is anything else that we can assist you with.

CLARK • COLLEGE

A PUBLICLY SUPPORTED
COMMUNITY COLLEGE

1800 E. McLOUGHLIN BLVD.
VANCOUVER, WA 98663
TELEPHONE (206) 694-6521

January 4, 1996

Lissi Hansen
15708 SE Evergreen Highway
Vancouver, WA 98684

Dear Ms. Hansen,

In regards to your letter of December 27, 1995, we would be delighted to assist you with your research. Please contact our office manager Claudia McHale at 992-2264 to schedule these appointments. We will supply any needed equipment and any necessaryy follow-up care for our students.

Please contact me directly should you need any further assistance.

Sincerely,

Mary Deal MSN, ARNP
Director of Health Services
Clark College

APPENDIX C

INFORMATION TO CLINIC SECRETARIES

Natalie Blizard
Office Manager
VA Employee Health
P. O. Box 1034
Portland, OR 97207

Dear Natalie Blizard,

When potential subjects for my master's research project, Effect of Hepatitis B Vaccine Temperature on Injection Pain, call to make an appointment for their hepatitis B vaccine immunization, I would like you to ask them, if they prior to the injection would like to speak to the nurse, Lissi who is going to give the injection regarding participating in a research study.

If the subjects ask, you may explain to them that the purpose of the research study is to compare the effect of two temperatures of the injected vaccine on pain. The subjects will not know the temperature of the vaccine they receive. The total time for participating including receiving the injection and rating their pain experience will take approximately 15-20 minutes.

You may inform the subjects that there is no risk associated with the study and that the nurse, Lissi will inform them further prior to participating in the research study if they choose to do so. Their participation does not cost anything and their identity will not be used for any publication or public purposes. Please, thank the subjects for calling and confirm their appointment.

Thank you for your help. If you have any questions or need additional information. Please, let me know.

Sincerely,

Lissi Hansen

Lissi Hansen

Valerie Andreas
Administrative Assistant
OHSU Employee Health
3181 S.W. Sam Jackson Park Road
Portland, OR 97201-3098

Dear Valerie Andreas,

When potential subjects for my master's research project, Effect of Hepatitis B Vaccine Temperature on Injection Pain, call to make an appointment for their hepatitis B vaccine immunization, I would like you to ask them, if they prior to the injection would like to speak to the nurse, Lissi who is going to give the injection regarding participating in a research study.

If the subjects ask, you may explain to them that the purpose of the research study is to compare the effect of two temperatures of the injected vaccine on pain. The subjects will not know the temperature of the vaccine they receive. The total time for participating including receiving the injection and rating their pain experience will take approximately 15-20 minutes.

You may inform the subjects that there is no risk associated with the study and that the nurse, Lissi will inform them further prior to participating in the research study if they choose to do so. Their participation does not cost anything and their identity will not be used for any publication or public purposes. Please, thank the subjects for calling and confirm their appointment.

Thank you for your help. If you have any questions or need additional information. Please, let me know.

Sincerely,

Lissi Hansen

Lissi Hansen

Claudia McHale
Office Manager
Clark College Health Services
1800 E. McLoughlin Blvd.
Vancouver, WA 98663

Dear Claudia McHale,

When potential subjects for my master's research project, Effect of Hepatitis B Vaccine Temperature on Injection Pain, call to make an appointment for their hepatitis B vaccine immunization, I would like you to ask them, if they prior to the injection would like to speak to the nurse, Lissi who is going to give the injection regarding participating in a research study.

If the subjects ask, you may explain to them that the purpose of the research study is to compare the effect of two temperatures of the injected vaccine on pain. The subjects will not know the temperature of the vaccine they receive. The total time for participating including receiving the injection and rating their pain experience will take approximately 15-20 minutes.

You may inform the subjects that there is no risk associated with the study and that the nurse, Lissi will inform them further prior to participating in the research study if they choose to do so. Their participation does not cost anything and their identity will not be used for any publication or public purposes. Please, thank the subjects for calling and confirm their appointment.

Thank you for your help. If you have any questions or need additional information. Please, let me know.

Sincerely,

Lissi Hansen

Lissi Hansen

APPENDIX D

CONSENT FORM

Department of Veterans Affairs

VA Research Consent Form

Subject Name: _____ Date: _____

Title of Study: Effect of Hepatitis B Vaccine Temperature on Injection Pain

Principal Investigator: Lissi Hansen, RN Graduate Student VAMC: _____

Description of Research By Investigator

PURPOSE

You have been invited to participate in this research study because you are going to receive an intramuscular injection of hepatitis B vaccine. The purpose of the study is to compare the effect of two temperatures of the injected vaccine on the amount of pain experienced at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection. One group of people will receive cool vaccine. The second group will receive room temperature vaccine. Selection into either group will be by chance, like flipping a coin. You will not know the group to which you are assigned.

PROCEDURE

Before your injection you will be interviewed about your previous experience with injections and other background information that will be used to describe the group of people being studied. The interview, the injection procedure, and your rating of the pain at the injection site will take approximately 20 minutes. At 5 seconds, 1 minute, 5 minutes, and 10 minutes after your injection, you will be asked to mark a pain rating scale and an unpleasantness scale that require brief responses.

RISKS AND DISCOMFORTS

This study involves a common intramuscular injection procedure. There is no cost to you to be in the study. You will receive your scheduled hepatitis B immunization whether or not you participate in the study. The injection may cause some local discomfort. There is no risk associated with the temperature of the hepatitis B vaccine whether it is given cool or at room temperature.

Subject's Identification (I.D. plate or give Name-last, first, middle)

Department of Veterans Affairs

VA Research Consent Form

Subject Name: _____ Date: _____

Title of Study: Effect of Hepatitis B Vaccine Temperature on Injection Pain

Principal Investigator: Lissi Hansen VAMC: _____

BENEFITS

You will not personally benefit from participating in this study. However, by serving as a subject, you may contribute new information which may benefit others in the future.

RIGHT TO WITHDRAW

Your participation in this research study is voluntary, and you may withdraw from this study at any time without prejudice to yourself or to any future medical care with this institution or with the Department of Veterans Affairs (VA). If you decline to participate in the study the investigator will administer the vaccine in usual manner. The investigator may exclude you from participating in the study at her discretion.

TREATMENT IN CASE OF INJURY

Every reasonable effort to prevent any injury that could result from this study will be taken. In the event of physical injuries resulting from the study, medical care and treatment will be available at this institution. For eligible veterans, compensation damages may be payable under 38 USC 251 or, in some circumstances, under the Federal Tort Claims Act. For non-eligible veterans and non-veterans, compensation would be limited to situations where negligence occurred and would be controlled by the provisions of the Federal Tort Claims Act. For clarification of these laws, contact District Counsel at (503) 326-2441. You have not waived any legal rights or released the hospital or its agents from liability for negligence by signing this form.

CONFIDENTIALITY

The result of your participation in this study may be used for publication or for scientific purposes, but your identity will not be disclosed unless you give separate, specific consent to this, or unless as required by law.

PARTICIPATION

Any individual participating in a study at the Department of Veterans Affairs Medical Center, Portland, Oregon is encouraged to contact Dr. Dennis J. Mazur, Chairman, Subcommittee on Human Studies, to discuss any issues related to their research study participation. Dr. Mazur can be reached through the Research Service (503) 220-8262 extension 6620.

Your signature below indicates that you understand that the Department of Veterans Affairs Medical Center, and your investigator of this research study bear no responsibility for any cost you may incur at other hospitals, clinics, or care institutions related to this study or to any of your medical conditions.

Department of Veterans Affairs

VA Research Consent Form

(Continuation Page 3 of 3)

Subject Name: _____ Date: _____

Title of Study: Effect of Hepatitis B Vaccine Temperature on Injection Pain

Principal Investigator: Lissi Hansen VAMC: _____

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above. Dr._____ has explained the study to me and answered all of my questions. I have been told of the risks and/or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of VA or other benefits to which I am entitled.

The results of this study may by published, but my records will not be revealed unless required by law.

In case there are medical problems or questions, I have been told I can call Dr._____ at _____during the day and Dr._____at_____after hours. If any medical problems occur in connection with this study the VA will provide emergency care.

I understand my rights as a research subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done. I will receive a signed copy of this consent form.

_____ _____
Signature of Subject Date

_____ _____
Signature of Witness Witness (print)

_____
Signature of Investigator

IF MORE THAN ONE PAGE IS USED, EACH PAGE (VAF 10-1086A) MUST BE CONSECUTIVELY NUMBERED AND SIGNED.

VA FORM
JAN 1990 10-1086

APPENDIX E

SUBJECT INFORMATION FORM

EFFECT OF HEPATITIS B VACCINE TEMPERATURE ON INJECTION PAIN

Lissi Hansen, BSN
Graduate Student
School of Nursing
Oregon Health Sciences University

What is the study about?

You have been invited to participate in this research study because you are going to receive an intramuscular injection of hepatitis B vaccine. The purpose of the study is to compare the effect of two temperatures of the injected vaccine on the amount of pain experienced at 5 seconds, 1 minute, 5 minutes, and 10 minutes after the injection. One group of people will receive cool vaccine. The second group will receive room temperature vaccine. Selection into either group will be by chance, like flipping a coin. You will not know the group to which you are assigned.

How will the study be done?

Before your injection you will be interviewed about your previous experience with injections and other background information that will be used to describe the group of people being studied. The interview, the injection procedure, and your rating of the pain will take approximately 20 minutes. At 5 seconds, 1 minute, 5 minutes, and 10 minutes after your injection, you will be asked to mark a pain rating scale and an unpleasantness scale that require brief responses.

The injection may cause some local discomfort. There is no risk associated with the temperature of the hepatitis B vaccine whether it is given cool or at room temperature. You may refuse to participate or you may withdraw from the study at any time without affecting your relationship with or treatment at the health clinic where you are receiving your immunization. You will receive your scheduled hepatitis B vaccine immunization whether or not you participate in the study

Who will be in the study?

People at least 18 years of age who need a hepatitis B vaccine. There is no cost to you or personally benefit to you from participating in the study. However, by participating you may contribute new information which may benefit others in the future. Neither your name nor your identity will be used for publication or publicity purposes. Your study records will be identified by a code number.

APPENDIX F

TEMPERATURE OF MEASURED

SALINE AND HEPATITIS B VACCINE

	Temperature (°F) of 1 ml 0.9% NS after removal from refrigerator			Temperature (°F) of 1 ml hepatitis B vaccine after removal from refrigerator		
Time	Trial #1	Trial #2	Trial #3	Trial #1	Trial #2	Trial#3
Rem. refrig.	44.4	44.4	42.2	41.4	43.6	43.3
15 sec.	44.6	44.8	42.8	41.8	44.0	43.7
30 sec.	45.4	45.7	44.5	42.4	44.5	44.0
45 sec.	46.3	46.5	45.8	43.0	45.2	45.5
1 min.	47.3	47.7	46.6	44.4	46.0	46.3
1.15 min.	48.4	48.6	47.5	45.1	47.0	47.8
1.30 min.	49.4	49.8	48.6	46.4	49.0	48.6
1.45 min.	50.4	50.5	49.8	47.0	49.9	49.4
2 min.	51.5	51.7	50.8	48.2	50.7	50.9
2.15 min.	52.3	52.6	51.7	48.8	51.4	51.5
2.30 min.	53.2	53.8	52.5	49.9	52.0	52.8
2.45 min.	54.5	54.2	53.2	50.4	53.0	53.5
3 min.	55.4	55.0	54.0	51.0	53.6	54.5
3.15 min.	55.7	55.7	54.8	52.0	54.5	55.4
3.30 min.	56.6	56.3	55.2	52.4	55.0	55.9
3.45 min.	57.0	56.8	55.8	53.4	55.8	56.8
4.00 min.	58.0	57.4	56.2	54.3	56.2	57.3
4.15 min.	58.5	58.0	56.9	54.7	57.4	58.0
4.30 min.	59.1	58.5	57.5	55.1	58.1	58.5
4.45 min.	59.5	59.2	58.1	55.9	58.5	59.1
5 min.	60.2	59.8	58.7	56.3	59.1	59.6
5.15 min.	60.6	60.3	59.2	57.0	59.5	60.2
5.30 min.	61.1	60.8	59.7	57.4	60.1	60.6
5.45 min.	61.5	61.1	59.9	58.1	60.3	61.2
6 min.	61.9	61.7	60.6	58.5	60.9	61.5
6.15 min	62.2	62.1	61.0	59.1	61.3	62.1
6.30 min.	62.7	62.7	61.5	59.5	61.8	62.4
6.45 min.	63.0	63.2	61.8	60.1	62.1	62.9
7 min.	63.4	63.6	62.3	60.6	62.7	63.2
7.15 min.	63.6	63.9	62.7	60.9	63.0	63.7
7.30 min.	64.3	64.2	63.3	61.2	63.4	63.9
7.45 min.	64.5	64.5	63.8	61.7	63.7	64.4
8 min.	64.7	64.9	64.1	62.0	64.2	64.9

(table continues)

	Temperature (°F) of 1 ml 0.9% NS after removal from refrigerator			Temperature (°F) of 1 ml hepatitis B vaccine after removal from refrigerator		
Time	Trial #1	Trial #2	Trial #3	Trial #1	Trial #2	Trial#3
8.15 min.	65.0	65.2	64.5	62.5	64.5	65.1
8.30 min.	65.2	65.6	64.8	62.9	64.8	65.3
8.31 min.	65.6	65.9	65.1	63.2	65.1	65.7
9 min.	65.9	66.2	65.4	63.4	65.5	66.0
9.15 min.	66.4	66.4	65.7	63.9	65.7	66.4
9.30 min.	66.7	66.6	66.1	64.1	66.1	66.5
9.45 min.	66.9	66.9	66.3	64.5	66.3	66.9
10 min.	70.3	70.2	66.9	64.7	66.7	67.1
10.15 min.	70.7	70.5	67.2	65.1	67.0	67.4
10.30 min.	71.0	70.9	67.5	65.3	67.3	67.6
10.45 min.	71.4	71.4	67.8	65.6	67.7	67.9
11 min.	71.6	71.7	68.0	65.8	67.8	68.1
11.15 min.	71.8	71.9	68.3	66.1	67.9	68.3
11.30 min.	72.0	72.1	68.6	66.3	68.2	68.5
11.45 min.	72.3	72.4	68.9	66.7	68.5	68.8
12 min.	72.7	72.7	70.3	67.0	68.6	68.9
12.15 min	73.0	72.9	70.6	67.1	68.9	69.2
12.30 min.	73.2	73.2	70.8	67.4	69.0	69.3
12.45 min.	73.5	73.4	71.2	67.5	69.3	69.5
13 min.	73.7	73.5	71.4	67.8	69.4	69.6
13.15 min.				67.9	69.4	69.8
13.30 min.				68.1	69.7	69.9
13.45 min.				68.3	69.8	70.1
14 min.				68.5	70.0	70.5
14.15 min.				68.6	70.2	70.7
14.30 min.				68.9	70.4	70.8
14.45 min.				69.1	70.5	71.0
15 min.				69.3	70.7	71.2
15.15 min.				69.5	70.9	71.4
15.30 min.				69.6	71.0	71.6
15.45 min.				69.8	71.2	71.7
16 min.				70.0	71.3	71.8
16.15 min.				70.1	71.4	71.9

(table continues)

	Temperature (°F) of 1 ml 0.9% NS after removal from refrigerator			Temperature (°F) of 1 ml hepatitis B vaccine after removal from refrigerator		
Time	Trial #1	Trial #2	Trial #3	Trial #1	Trial #2	Trial#3
16.30 min.				70.2	71.5	72.1
16.45 min.				70.3	71.6	72.2
17 min.				70.5	71.8	72.3
17.15 min.				70.6	71.9	72.4
17.30 min				70.8	72.0	72.6
17.45 min.				71.0	72.1	72.7
18 min.				71.1	72.2	72.8
18.15 min.				71.2	72.3	72.9
18.30 min.				71.3	72.5	73.1
18.45 min.				71.5	72.6	73.3
19 min.				71.6	72.7	73.4
19.15 min.				71.8	72.8	
19.30 min.				71.9	72.9	
19.45 min.				72.0	73.1	
20 min.				72.2	73.2	
20.15 min.				72.3	73.3	

APPENDIX G

TEMPERATURE OF MEASURED

HEPATITIS B VACCINE IN SYRINGES

AND

ADMINISTRATION TIME

Temperature of measured hepatitis B vaccine in syringes which have been refrigerated for a minimum of 24 hours prior to use

Steps in procedure	Trial # 1	Trial # 2	Trial # 3
Disinfect top of hepatitis B vaccine vial with 70% isopropyl alcohol and to let it dry takes 10 seconds.			
Draw hepatitis B vaccine into "cold" syringe takes 15 seconds.			
Remove plunger and place electronic pocket digital thermometer in center of "cold" syringe.			
Temperature of hepatitis B vaccine 30 seconds after removal from refrigerator:	43.9°F	43.0°F	44.2°F
60 seconds after removal from refrigerator:	46.9°F	45.5°F	47.1°F
90 seconds after removal from refrigerator:	49.0°F	48.5°F	49.2°F

Length of time in seconds from removal of hepatitis B vaccine from the refrigerator and until it has been administered

Steps in procedure	Trial # 1	Trial # 2	Trial # 3
Remove hepatitis B vaccine from refrigerator:	3	3	3
Disinfect top of vial with 70% isopropyl alcohol:	13	13	12
Draw vaccine into syringe:	11	10	9
Remove air bubbles:	11	11	10
Change needle:	7	8	8
Fill needle with vaccine:	4	3	4
Go to exam room:	9	9	8
Determine injection site:	4	4	4
Administer vaccine (injection + aspiration):	11	11	12
	73	72	70

APPENDIX H

ROOM TEMPERATURES

Room Temperatures (°F)

Day	8 AM	10 AM	12 Noon	2 PM	4 PM
			Clark College Health Services		
Tuesday:	74.2	74.2			
Wednesday:	73.6	73.7	73.8	74.1	74.4
Thursday:	73.6	74.1	74.2	74.2	74.1
Refrigerator Temperature (°F): Approximately 38					
			VA Employee Health Clinic		
Thursday:			71.5	71.6	71.6
Friday:	73.0		72.7	72.7	
Monday:	71.8	72.2	72.2		
Refrigerator Temperature (°F): Approximately 40					
			OHSU Employee Health Clinic		
Wednesday:	72.6	72.7	72.7	72.6	
Refrigerator Temperature (°F): Approximately 41					

APPENDIX I

DATA COLLECTION BOOKLET

Data Collection Form Booklet

Hepatitis B Vaccine Temperature Study

Lissi Hansen
1996

ID #: _____
Date: _____
Site: _____

Hepatitis B Vaccine Temperature Study

Information Sheet ID #: _____

1. Age:_____

2. Gender:
   1. ( ) Female
   2. ( ) Male

3. Marital Status:
   1. ( ) Single
   2. ( ) Married
   3. ( ) Separated
   4. ( ) Divorced
   5. ( ) Widowed
   6. ( ) Other

4. Ethnicity:
   1. ( ) Caucasian
   2. ( ) Black/African American
   3. ( ) Native American
   4. ( ) Hispanic
   5. ( ) Asian/Pacific Islander
   6. ( ) Other

5. Highest Grade Completed:
   1. ( ) Less than high school education
   2. ( ) High school education or equivalent
   3. ( ) College courses
   4. ( ) 4-year college degree
   5. ( ) Post graduate education

6. Occupation:_____

7. Number of intramuscular injections in the past year:_____

8. This is hepatitis vaccine number:
   1. ( ) 1
   2. ( ) 2
   3. ( ) 3

9. Problems with injections in the past: ID #:_____

1. ( ) None
2. ( ) Tenderness
3. ( ) Redness
4. ( ) Swelling
5. ( ) Bruising
6. ( ) Bleeding
7. ( ) Other: _____

10. Exclusion criteria:

Yes	No	
( )	( )	Allergy to yeast or thimerosal (mercury derivative)
( )	( )	Frequent intramuscular injections - 5 or more in the past year
( )	( )	Inability to understand English
( )	( )	Unable to consent
( )	( )	Blood aspirated in syringe
( )	( )	Physically unable to mark pain intensity and unpleasantness scale
( )	( )	Pregnancy (Administered only if clearly needed, e. g. high risk)
( )	( )	Breast feeding (May be excreted in human milk)
( )	( )	Other:_____

11. Injection Information:

Group I: ( ) Cool vaccine
Group II: ( ) Room temperature vaccine

Date:_____
Time:_____

Site: ( ) Left Deltoid Muscle
( ) Right Deltoid Muscle

Needle length ( ) 5/8 inch
( ) 1 inch
( ) 1 ¼ inches
( ) 1 ½ inches

12. Comments:

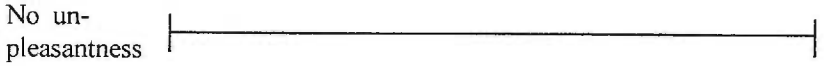
ID#: _____

PAIN & UNPLEASANTNESS RATING SCALES

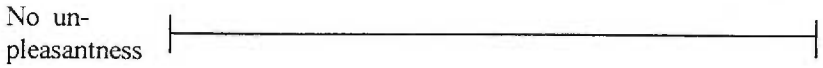
Place a vertical mark on the line that best describe your pain intensity and pain unpleasantness experience.

I. After 5 seconds:

II. After 1 minute:



III. After 5 minutes:

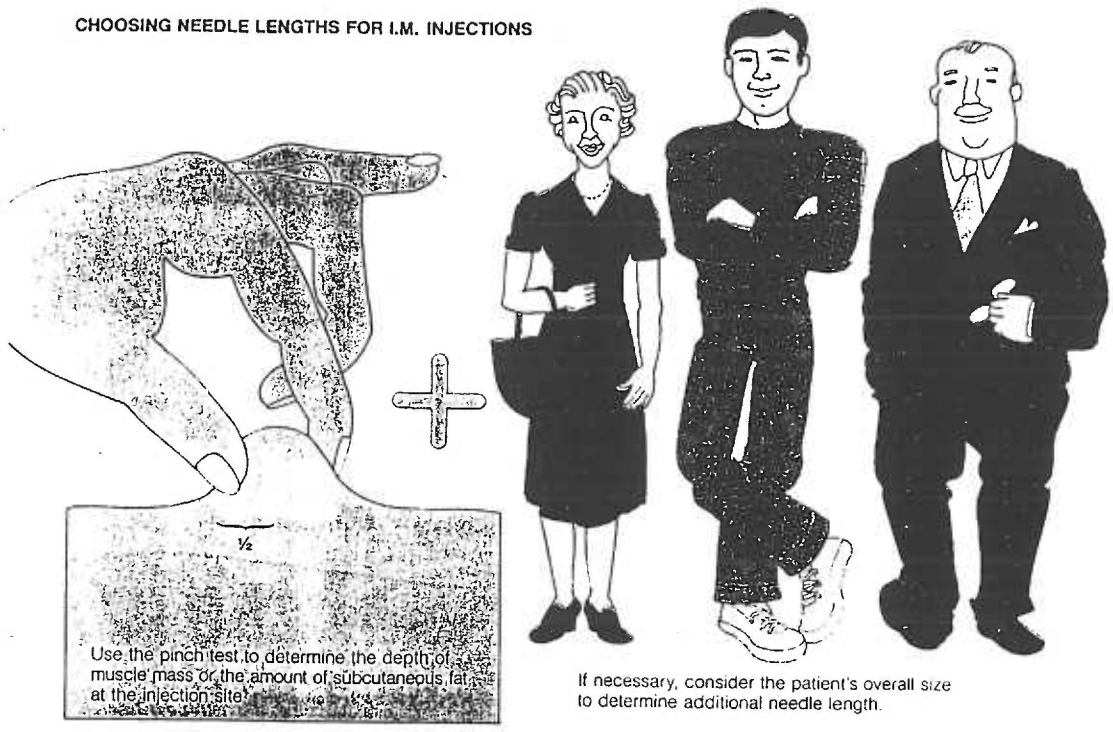


IV. After 10 minutes:

APPENDIX J

PINCH TEST

The Pinch Test



Note. From "Make your needle selection right to the point," by C. L. Lenz, 1983, RN, 13, p. 50.

APPENDIX K

DATA COLLECTION PROTOCOL

DATA COLLECTION PROTOCOL

Obtain Subjects

1. Obtain names of individuals scheduled for hepatitis B vaccine injections at the health clinics from the clinic secretaries.
2. In advance, assign subjects to one of the two treatment groups.
    a. One die will be thrown for each potential subject at each study site prior to the first data collection day at each health clinic.
    b. If an even number shows, the subjects will be assigned to study Group I.
    c. If an odd number shows, the subjects will be assigned to study Group II.
    d. Subjects will be blind to their assigned group.
3. Subjects in Group I will receive cool hepatitis B vaccine (approximately 9.4°C [49°F]). The vial with vaccine will be left in the refrigerator until the immediate time of injection.
4. Subjects in Group II will receive room temperature hepatitis B vaccine. The vial with vaccine will be taken out of the refrigerator a minimum of 21 minutes prior to use and kept at room temperature (approximately 22.8°C [73°F]).
5. Assign sequential ID number to each subjects.
6. Subjects will receive their hepatitis B vaccine in a room different from the one where the refrigerator is located to conceal whether cool vaccine or vaccine at room temperature will be administered.
7. When subjects present themselves in the health clinics, the investigator will greet them by name and say, "My name is Lissi, and I am the nurse who is going to give you your hepatitis B vaccine. Please follow me to the examination room."
8. Show subjects to a chair and ask them to please have a seat. When sitting down the investigator continues by saying. "As I mentioned, I am a nurse, but also a graduate student at the Oregon Health Sciences University School of Nursing and am currently conducting a research study on the effect of two temperatures of injected hepatitis B vaccine on injection pain. I am asking if you would like to participate in this study. It will take approximately 15 minutes. Before you make up your mind, I would like you to read this information form (or consent form). This will give you an explanation about the study. I will leave the room for 3 minutes or so, so you can read the information form (or consent form) without me disturbing you. After you have read the information form (or consent form), I will answer any questions you may have." Subjects at the VA Employee Health Clinic will be provided with a consent form (see Appendix D). Subjects at OHSU Employee Health Clinic and at Clark College Health Services will be provided with a subject information form (see Appendix E).
9. Leave examination room for approximately 3 minutes.
10. Return to the examination room after approximately 3 minutes and sit down.
11. Address potential subject. "Do you have any questions after you read the information form (or the consent form)?" Answer any questions the potential subject may have. Ask the subject, "Would you like to participate in this study?"
    If affirmative, the VA Employee Health Clinic subject's signature will be obtained on the consent form witnessed by the clinic secretary. The investigator will sign and date the consent form below the subject's signature.

Obtain Background Information

1. The investigator continues by saying, "Before I give you your hepatitis B vaccine injection, I am going to ask you some background information and information about your previous experience with injections (see Appendix I)
   Ask subject about age. Record subject's age.
   Ask subject about marital status. Record subject's marital status.
   Ask subject about ethnicity. Record subject's ethnicity.
   Ask subject about highest grade completed. Record subject's highest grade completed.
   Ask subject about occupation. Record subject's occupation.
   Ask subject about number of intramuscular injections in the past year. Record subject's number of intramuscular injections in the past year.
   Ask subject, "Is this your first hepatitis B vaccine injection?
   If it is hepatitis B vaccine injection number 1, obtain subject's signature on health clinic's "Informed Consent for Hepatitis B Vaccine."
   Ask subject, "Is this your hepatitis B vaccine injection number 2?
   Ask subject, "Is this your hepatitis B vaccine injection number 3?
   Record the number of the hepatitis B vaccine to be administered.
2. Verify subject's name and medication to be administered
3. Ask subject about problems with injections in the past. Record subject's problems with injections in the past.
4. Ask subject about exclusion criteria. Record subject's exclusion criteria.
5. Record date and time.
6. Ask subject if she/he prefers the injection in left or right deltoid muscle. Record the left or right site of injection.
7. Investigator shows location of the deltoid muscle on herself.
8. Record any comments.
9. Instruct subject how to complete the pain intensity scale and pain unpleasantness scale by saying, "After your hepatitis B vaccine injection, I will place a dry cotton ball over the injection site immediately after the injection. I will hold the dry cotton ball over the site for 3-4 seconds. At the same time, I will ask you to rate the pain intensity and the pain unpleasantness scales. The pain intensity scale refers to the intensity of the pain which you are experiencing whereas the pain unpleasantness scale refers to how unpleasant the pain is; how much the pain bothers you. I want you to think of the pain intensity and its unpleasantness as two separate things and measure them on the pain intensity scale and the pain unpleasantness scale respectively. The far left side of the pain intensity scale and the pain unpleasantness scale represent "no pain or no unpleasantness" whereas the far right side of the scales represent "pain as bad as it could be or unpleasantness as bad as it could be. Place a vertical mark on the scales at the point representing the pain intensity and pain unpleasantness you are experiencing at the indicated time intervals. The first time after 5 seconds, the second time after 1 minute, the third time after 5 minutes, and the last time after 10 minutes. I have an example to show you. The scales, I want you to rate, look like these." Show the subject the hunger and unpleasantness of hunger rating scales (see example on p. 88).

"As the pain intensity and pain unpleasantness scales, the hunger intensity and unpleasantness of hunger scales indicate "no hunger or no unpleasantness of hunger" to the far left side of the scales, whereas the far right side represents "hunger as bad as it could be or unpleasantness of hunger as bad as it could be." These scales are also rated by placing a vertical mark at the point that best represents hunger intensity and hunger unpleasantness experience."

10. "After 5 seconds when you have rated the first two scales, a tape-recorder will be played indicating the three additional times I would like for you to rate your pain intensity and pain unpleasantness experience. Between the 5 seconds ratings and the 1 minute ratings, I will place a small band-aid over the injection site to prevent any minute amount of blood if it should be present to stain your clothing. Then I will discard the cotton ball, syringe, and needle and leave the room. I will return after you have completed the scales. During the time you are participating in this study and sitting in this examination room you are welcome to look in the magazines on the table. If you brought your own reading material, you are welcome to read in it."

Explain the Procedure

1. "Before I give you your hepatitis B vaccine injection, I will ask you to sit on the examination table or on the chair next to me. To get an estimate of the amount of subcutaneous fat over your deltoid muscle, I will feel the subcutaneous fat over it by lightly pinching it between my thumb and index finger. I will do this on the opposite site of where you will receive the injection. First I will ask you to lift up your sleeve or take your arm out of your blouse/shirt on the site where I will do the estimate, and then I will ask you to do the same on the side where you are going to receive the injection, so I can disinfect the injection area. I will use alcohol which I will let dry for a minute or so while I leave the room to get your vaccine. When I come back, I will give you your injection and place the dry cotton ball over its site as mentioned. Do you have any questions?"

Administer Intramuscular Injection

1. Ask subject to sit on examination table (preferably) or chair next to the investigator.
2. Ask subject to remove clothing from the shoulder where the hepatitis B vaccine will not be administered. Lightly pinch the subcutaneous fat over the deltoid muscle area between the thumb and index finger. One half of the distance between the thumb and index finger will be the approximately length of the needle required to reach into the deltoid muscle. For adults, suggested needle length is 1 to 1 ½ inches. Twenty five gauge needles will be used.
3. Ask subject to remove clothing from the shoulder where the hepatitis B vaccine injection will be administered.
4. Have subject remove as little clothing as possible to protect her/his privacy.
5. Place a pen and a clipboard containing the VASs next to the subject.
6. Place a dry cotton ball and a small band-aid close to the subject and within reach of the investigator.
7. Have tape recorder ready and within reach of the investigator.
8. Ask subject to slightly bend the preferred arm at the elbow and rest it on the thigh.

9. Locate deltoid muscle injection site: palpate the lower edge of the acromion process at the tip of the shoulder. Locate the point below on the lateral aspect of the arm in line with the top of the axilla. The recommended boundaries of the injection are within the upside-down triangle between the lower edge of the acromion and the point on the lateral aspect of the arm in line with the axilla.
10. Cleanse skin at the injection site with 70% isopropyl alcohol in a circular fashion and allow it to dry 70 to 90 seconds.
11. Leave room and go to other examination room where the hepatitis B vaccine is stored.
12. If subject assigned to Group I: take the vial (at OHSU Employee Health Clinic take two .5 ml vials) and a 3 ml sterile syringe from the refrigerator immediately prior to administration, shake the vial (vials) and withdraw the 1 ml hepatitis B vaccine into the syringe, using aseptic technique.
13. If subject assigned to Group II: take the vial (at OHSU Employee Health Clinic take two .5 vials) left at room temperature, shake it (them) and withdraw the 1 ml hepatitis B vaccine into a 3 ml sterile syringe, using aseptic technique. (Agitation at the time of administration is necessary to maintain suspension of the vaccine).
14. Change needle to prevent tracking hepatitis B vaccine through the subcutaneous tissue. Carefully remove and discard needle used to withdraw the hepatitis B vaccine and change to a sterile 25-gauge 5/8 inch to 1 ½ inches long needle as determined by the pinch test. Fill needle with vaccine.
15. Return to room.
16. Locate and support deltoid muscle between the left hand's thumb and fingers to stabilize the muscle and stretch the skin at the injection site.
17. Insert needle quickly at a 90° angle to the skin into the body of the deltoid muscle about three fingers breadth (or about 1 to 2 inches) below the acromion.
18. Once the needle is inserted, release the support of the deltoid muscle and place the left hand's thumb and fingers on the syringe. Aspirate to check for blood return (3 to 5 seconds). If blood returns into the syringe, withdraw the needle and start over. Delete the subject from the study.
19. Inject vaccine over approximately 5 seconds.
20. Withdraw needle smoothly after 4 to 5 seconds (injection finished), and lightly place a dry cotton ball over the injection site without pressure for 3 to 4 seconds.
21. Ask subject to take the pen and clipboard containing the VAS and to mark the two VAS under number 1 (after 5 seconds).
22. Start tape recorder and play tape to indicate when subject has to mark VAS under number 2, 3, and 4 (after 1 minute, 5 minutes, and 10 minutes).
23. Apply small band-aid over injection site.
24. Discard cotton ball and place needle and syringe in sharp container.
25. Record length of needle used and injection site in data collection form.
26. Leave examination room to allow time and privacy for subject to complete the scales.
27. Return approximately 9 minutes later and thank subject for participating in the study.
28. At the VA Employee Health, inquire if subject wants copy of consent. If affirmative, give copy of consent form to the subject, retain another copy, and place original copy in subject's file.
29. Record whether subject was assigned to Group I or II in data collection booklet.

ID #: _____

HUNGER & UNPLEASANTNESS OF HUNGER RATING SCALES

Place a vertical mark on the line that best describe your hunger intensity and hunger unpleasantness experience.

I. After 5 seconds:

No hunger ——————————— Hunger as bad as it could be

No unpleasantness of hunger ——————————— Unpleasantness of hunger as bad as it could be

II. After 1 minute:

No hunger ——————————— Hunger as bad as it could be

No unpleasantness of hunger ——————————— Unpleasantness of hunger as bad as it could be

III. After 5 minutes:

No hunger ——————————— Hunger as bad as it could be

No unpleasantness of hunger ——————————— Unpleasantness of hunger as bad as it could be

IV. After 10 minutes:

No hunger ——————————— Hunger as bad as it could be

No unpleasantness of hunger ——————————— Unpleasantness of hunger as bad as it could be

APPENDIX L

QUESTIONS PROVIDED TO SUBJECTS

IN PILOT STUDY

Questions regarding the VAS as pain intensity rating scale and the VDS as pain unpleasantness rating scale when presented on one page:

1. What do you think of the pain intensity and pain unpleasantness rating scales?
2. Would you have liked to have had the same kind of rating scale for the two ratings?
3. How was it to rate your pain intensity and pain unpleasantness when you had all your scores available to look at during the ratings?
4. Would you have liked not to have had all your scores available to look at during the ratings?
5. Were the rating scales equally easy to rate?
6. Were the rating scales clearly made?
7. How was the explanation and the information about the rating scales you received prior to the injection?
8. Anything else you would have liked to have known about the rating scales?

Questions regarding the VAS as pain intensity and pain unpleasantness rating scale when presented on one page:

1. What do you think of the pain intensity and pain unpleasantness rating scale?
2. Would you have liked to have had two different rating scales for the two ratings?
3. How was it to rate your pain intensity and pain unpleasantness when you had all your scores available to look at during the ratings?
4. Would you have liked not to have had all your scores available to look at during the ratings?
5. Was the rating scale clearly made?
6. How was the explanation and the information about the rating scale you received prior to the injection?
7. Anything else you would have liked to have known about the rating scale?

Questions regarding the VAS as pain intensity and the VDS as pain unpleasantness rating scales when presented on 4 separate pages:

1. What do you think of the pain intensity and pain unpleasantness rating scales?
2. Would you have liked to have had the same kind of rating scale for the two ratings?
3. How was it to rate your pain intensity and pain unpleasantness when you did not have all your scores available to look at during the ratings?
4. Would you have liked to have had all your scores available to look at during the ratings?
5. Were the rating scales equally easy to rate?
6. Were the rating scales clearly made?
7. How was the explanation and the information about the rating scales you received prior to the injection?
8. Anything else you would have liked to have known about the rating scales?

Questions regarding the VAS as pain intensity and pain unpleasantness rating scale when presented on 4 separate pages:

1. What do you think of the pain intensity and pain unpleasantness rating scale?
2. Would you have liked to have had two different rating scales for the two ratings?
3. How was it to rate your pain intensity and pain unpleasantness when you did not have all your scores available to look at during the ratings?
4. Would you have liked to have had all your scores available to look at during the ratings?
5. Was the rating scale clearly made?
6. How was the explanation and the information about the rating scale you received prior to the injection?
7. Anything else you would have liked to have known about the rating scale?