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AN INEXPENSIVE HEAD RESTRAINT SYSTEM FOR LONG TERM INTRAVENOUS ADMINISTRATION OF DRUGS IN THE MONKEY

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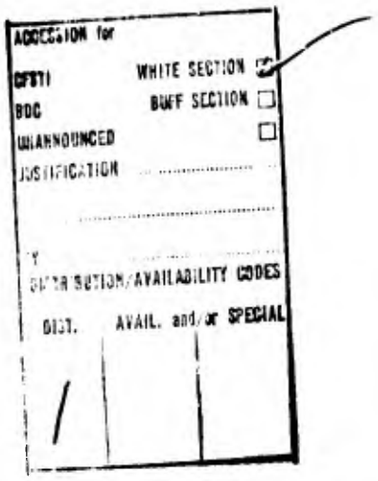
The animals used in this study were handled in accordance with the "Guide for Laboratory Animal Facilities and Care" as promulgated by the National Academy of Sciences - National Research Council.



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FOREWORD

This work was accomplished at the 6571st Aeromedical Research Laboratory, Holloman Air Force Base, New Mexico, as part of a joint effort by the Air Force and the Food and Drug Administration under Project 6893, Task 02, in conjunction with the Abuse and Liabilities Branch, Division of Drug Studies and Statistics.

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This technical report has been reviewed and approved for publication.

C. H. KRATOCHVIL, Colonel, USAF, MC
Commander

ABSTRACT

A head restraint system allowing intravenous administration and self-administration of compounds in monkeys under conditions of minimal restraint is described. The system has functioned well even with large male Macaques and requires no handling of the subjects for administration of drugs. Additional advantages of the present system, its ease of fabrication, light weight, and low cost are discussed.

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I

INTRODUCTION

A study in progress requires that monkeys (Macaca species) be implanted with a chronic in-dwelling catheter through which drugs may be administered under conditions of minimal restraint and without handling the animal. Although complex and multipurpose head restraint systems do exist[1], a relatively lightweight, inexpensive and easily fabricated system has been developed which admirably fulfills this requirement. To date, Macaca iris and Macaca mulatta subjects weighing up to 8.62 kg. (19 lb.) have been fitted to the restraint system without complications.

II

METHOD

A. APPARATUS

The restraining unit (Fig. 1) consists of a skull plate, spring, Plexiglas lock washers, appropriate size bolts and screws, silicone rubber catheter, and attachment hardware.

Skull plate -- The skull plate is constructed of .0250 gauge stainless steel cut in a cloverleaf design. Each of the radiating appendages is slotted. To this base a 7/16-inch stainless steel pressure-line connector is silver soldered. A hole is then drilled in the base plate under the pressure connector to permit passage of a catheter through the headpiece.

Spring -- A number 4 screen door spring[2] connected from the head plate to the side of the cage is used to protect

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[1] Findley, Jack. Personal communication. Institute of Behavioral Research, Silver Spring, Maryland, 1967.

[2] Moderately tempered steel spring approximately 40 cm. in length containing approximately eight coils per cm.

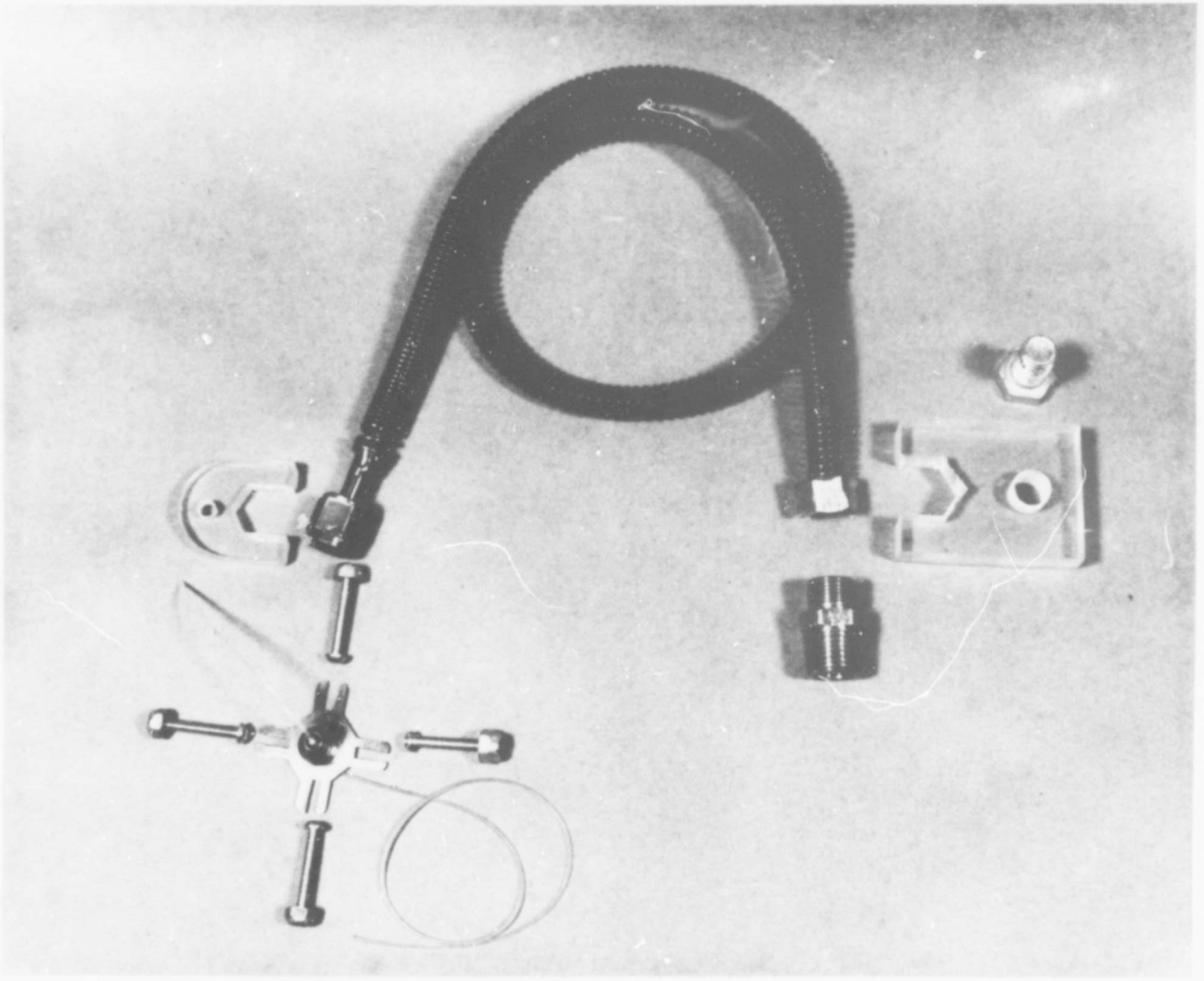

Figure 1. Restraint Unit Components and Hardware

the catheter. After a 7/16-inch nut has been brazed to each end of the spring, the spring can be stretched sufficiently to permit freedom of movement in the cage.

Plexiglas lock washers -- A Plexiglas washer connected between the assembled restraint spring and anchor bolts set in the subject's skull is employed to insure that sudden jolts will not loosen the restraint connection. Another lock washer constructed of 1/2-inch Plexiglas is used to attach the spring to the side of the cage and prevent the spring from rotating as the animal moves. It is 2 inches long, 1-1/2 inches wide, and drilled and threaded to accommodate a large bolt. A notch is cut on one end to fit the nut on the end of the spring.

Silicone rubber tubing -- A single length of silicone rubber tubing[3] extends from the infusion pump outside the cage into the animal's jugular vein. The size of the tubing used in this study is .041-inch outer diameter by .020-inch inner diameter. The silicone rubber tubing is prepared for implantation by first sealing one end with silicone rubber[4] and then puncturing the tubing in several places with a hypodermic needle just above the seal. This technique prevents the formation of clots at the end of the catheter.

B. PROCEDURE

A monkey is removed from its cage and anesthetized for catheterization and placement in the head restraint apparatus. An incision is made in the subject's neck and the silicone rubber tubing is inserted into the external jugular vein.

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[3] Vivosil, medical grade, Becton-Dickenson and Company, Rutherford, New Jersey.

[4] RTV-102, silicone rubber, General Electric Company, Waterford, New York.

The tubing is then extended subcutaneously to an incision at the dorsal midline of the head. Below this incision, modified trepanations in the form of keyholes are made to align with the slots on the skull plate (care should be taken to avoid penetration of the dura). The tubing is then passed through the hole in the center of the skull plate. A bolt is inserted into each keyhole slot with the head of the bolt under the skull. Nuts are turned down on the bolts, thus anchoring the skull plate to the subject. One long bolt is left protruding from the skull for later additional use as a lock washer anchor. Any exposed bone, the radiating appendages of the skull plate, and the anchoring nuts are then overlaid with Kadon dental cement.[5] Care must be taken to avoid applying cement to the threaded part of the base plate.

To place the animal in the restraint apparatus, the silicone tubing extending from the animal's head is threaded through the spring. The nut brazed on the end of the spring is then tightened on the skull plate. A lock washer that prevents sudden jolts from loosening the spring is then placed over the spring nut and attached to protruding skull plate anchor bolts. The spring is attached to the side of the cage by means of the Plexiglas lock washer and a flanged retaining nut outside the cage (Fig. 2).

C. APPLICATIONS AND LIMITATIONS

This apparatus has been specifically designed to study the abuse liability of certain drug compounds by permitting a subject to inject itself under conditions of minimal restraint. It has the additional advantages of being inexpensively constructed from readily available parts and easily assembled in a small shop. Hardware of other sizes and materials could be substituted for that described.

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[5] Kadon Dental Cement, The L. D. Caulk Company, Milford, Delaware.

Figure 2. Macaca Mulatta in Restraint Apparatus

Occasionally a coil will develop in the spring, thus shortening it by several inches. This is easily corrected by loosening the Plexiglas lock washer which anchors the spring to the cage and rotating the spring until it uncoils. If it becomes necessary to handle the animal, the spring-to-cage lock washer may be loosened and the spring retracted outside the cage, thus immobilizing the subject's head against the side of the cage.

Close observations over a period of 8 weeks have indicated that Macaques adapt quickly to the head restraint apparatus. Following an initial period of investigation, they tend to disregard the spring and move freely about their cages. The spring and head plate system has effectively withstood the stress imposed during displays of aggression and other nervous behavior characteristics of the Macaques.

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