AL-NAKEEB, Shaheen Mustafa, 1939-
DEVELOPMENT AND EVALUATION OF A THORACIC
PERCUTANEOUS LEAD SYSTEM.

Iowa State University, Ph.D., 1969
Engineering, biomedical

University Microfilms, Inc., Ann Arbor, Michigan

THIS DISSERTATION HAS BEEN MICROFILMED EXACTLY AS RECEIVED
DEVELOPMENT AND EVALUATION
OF A THORACIC PERCUTANEOUS LEAD SYSTEM

by

Shaheen Mustafa Al-Nakeeb

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Veterinary Pathology

Approved:

Signature was redacted for privacy.
In Charge of Major Work

Signature was redacted for privacy.
Head of Major Department

Signature was redacted for privacy.
Dean of Graduate College

Iowa State University
Ames, Iowa
1969
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>LITERATURE REVIEW</td>
<td>3</td>
</tr>
<tr>
<td>Artificial Organs and Lead Systems</td>
<td>3</td>
</tr>
<tr>
<td>Prosthetic Materials</td>
<td>7</td>
</tr>
<tr>
<td>Silicone</td>
<td>9</td>
</tr>
<tr>
<td>Polytetrafluoroethylene (Teflon)</td>
<td>13</td>
</tr>
<tr>
<td>Tissue Reactions to Silicone and Teflon</td>
<td>16</td>
</tr>
<tr>
<td>MATERIALS AND METHODS</td>
<td>19</td>
</tr>
<tr>
<td>The Lead System</td>
<td>19</td>
</tr>
<tr>
<td>Experimental Animals</td>
<td>23</td>
</tr>
<tr>
<td>Anesthesia and Presurgical Preparations</td>
<td>24</td>
</tr>
<tr>
<td>Surgical Anatomy and Technique</td>
<td>25</td>
</tr>
<tr>
<td>RESULTS</td>
<td>27</td>
</tr>
<tr>
<td>Group 1: 30 Days Observation Period</td>
<td>27</td>
</tr>
<tr>
<td>Group 2: 90 Days Observation Period</td>
<td>43</td>
</tr>
<tr>
<td>Group 3: 210 Days Observation Period</td>
<td>57</td>
</tr>
<tr>
<td>Group 4: 365 Days Observation Period</td>
<td>68</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>82</td>
</tr>
<tr>
<td>SUMMARY AND CONCLUSIONS</td>
<td>90</td>
</tr>
<tr>
<td>BIBLIOGRAPHY</td>
<td>94</td>
</tr>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>100</td>
</tr>
</tbody>
</table>
INTRODUCTION

Heart and lung diseases are being treated or corrected by various medical and surgical methods. Extensive research is in progress to assist or replace severely damaged organs such as hearts, lungs, kidneys, and livers. Organ transplantation research has the unsolved tissue rejection problem and the lack of adequate sources of organs suitable for transplant. The recently used methods of immunological tolerance induction lack specificity; and until these methods are controlled, organ transplantation will not be fully acceptable.

The advancement of technology, multidisciplinary cooperation and team efforts provide an optimistic future for artificial organs. Artificial hearts and artificial lungs may be the future answer for patients with incurable heart and lung diseases. However, the mechanical heart research area also has a number of areas of needed study such as device design, power supplies, control systems, blood flow studies and suitable long-term percutaneous leads.

Considerable work has been done on percutaneous leads in the past, especially in conjunction with artificial kidney dialysis. As the mechanical heart studies move from the acute to the chronic phases, new and improved percutaneous leads are an absolute requirement. Without these, refined mechanical devices, power systems, and control mechanisms will all be ineffective for use over prolonged periods of time.
The purpose of this investigation was to design and evaluate a thoracic percutaneous lead system so that it could contain tubes for fluids, air and/or electrical leads that could be utilized in either implanted or external circulatory assist devices. Two of the best inert synthetic polymers were used in construction of the lead system. Tissue reactions to the lead system and the effect of a pulsating device on tissue were studied. Stability of the device and control of infection were all taken into account.
LITERATURE REVIEW

Artificial Organs and Lead Systems

On December 3, 1967, a milestone was laid in the history of medicine when Dr. Christiaan Barnard of Groote Schuerr Hospital in Cape Town, South Africa, implanted a heart in Louis Washkansky, who survived only 18 days. Another patient of Dr. Barnard's, Philip Blaiberg, survived for 19-1/2 months. Of the 148 patients who have received transplanted hearts, only 31 are living at the present time.

Since the heart-lung machines and techniques of organ transplantation have been worked out successfully, the low survival rate is attributed mainly to immunological incompatibility. The use of immunosuppressive drugs and agents in organ transplantation has increased the tolerance of organs. Corticosteroids, x-ray irradiation, azathioprine and antilymphocytic globulins are used as immunosuppressive agents. However, these agents are non-specific, toxic and will reduce the recipient's resistance to bacterial infection.

According to Nossal (1969), an overwhelming array of practical problems in tolerance induction in organ transplantation should be solved before its realistic clinical application. Of those problems, purification and characterization of transplant antigens; duration of tolerance; source of antigens and risk of some immunization are to be controlled in tolerance induction before attempting wide
clinical use of organ transplantation. The author advocates that it is too early for human experimentation in this field.

Until the immunological problems are solved, the artificial organs seem to be the hope for transplantation demanding patients. Artificial organs also have problems which need to be solved before clinical application. However the search for artificial organs is one of continuing progress. The majority of artificial hearts or heart assists are designed on the principle of a pump. Some are designed to replace the heart while others support the diseased organ. According to Hall et al. (1967), the main problem areas in developing artificial hearts and assistors are pump design, materials research and pump control.

Reports on artificial hearts are numerous in this decade's literature; Hastings et al. (1961), Liotta et al. (1961), Akutsu et al. (1963, 1965), Topax (1964), Kirby et al. (1964), Grädel et al. (1965), Cholvin et al. (1965), Nosé et al. (1965), Pierce et al. (1965), Woodward et al. (1966), Hall et al. (1967), and Wildevuur et al. (1968).

There are various types of energy coupling systems used to drive the artificial hearts; Hall et al. (1967) stated that hydraulic systems are being most commonly used. Gas or liquid are also used, gas being more acceptable.

Bodell et al. (1965) reported on initial experiments on implantable artificial lungs which consisted of a
teflon\textsuperscript{1} arterial graft filled with silicone rubber\textsuperscript{2} capillary tubing. The capillary tubing was brought through the teflon graft by two tubes for oxygenation and removal of carbon dioxide. This artificial lung was implanted between the pulmonary artery and the left auricle. A definite change in arterial blood oxygen tension was noticed in 7 of the 10 sheep and dogs used. Coagulation of blood within the artificial lung was the main problem of this study.

Stewart and Baretta (1968) reported on an artificial capillary lung which was basically similar to the previous one. Silastic\textsuperscript{3} capillaries were placed in a plastic cylinder. Blood was introduced and removed from the silastic capillaries by silastic tubes and oxygen was flowed through the jacket surrounding the capillaries. The artificial lung was placed in a shunt between the femoral veins in dogs.

There is great need for lead systems, which will carry the required external energy, control mechanisms, monitoring wires, transducers and tubes to the artificial organs within the thoracic cavity. Various materials have been used in lead systems for monitoring physiological functions of organs.

\textsuperscript{1}E. I. DuPont de Nemours and Company, Wilmington, Delaware.

\textsuperscript{2}Dow Corning, Inc., Midland, Michigan.

\textsuperscript{3}Dow Corning, Inc., Midland, Michigan.
Cholvin (1961) described lead systems which were used for experimental physiology. A teflon skin grommet was implanted in dogs at the mid-dorsal thoracic region posterior to the scapula. Various forms of electronic lead wires, connecting multiple transducers, passed through the grommet to implantation beds in the subcutis, ribs and intrathoracic sites. The grommet was well tolerated in dogs up to 21 months. Electrocardiograms, phonocardiograms and respiration were monitored with the multiple transducer system. In evaluating 15 forms of polymers and metals in chronic implantation studies, the author reported that teflon and silicones were the most inert of the materials tested.

Vasko and Rawson (1967) reported on a non-reactive, chronic, percutaneous lead system. A button was molded from medical grade silicones. A hole was made on the narrow surface of the button to exteriorize the leads and a cuff of dacron felt was applied around the neck and the lower portion of the button to allow tissue ingrowth. This lead system was used in dogs, guinea pigs, sheep and primates. Although satisfactory results were obtained with this implant, some implants were extruded by the host because of infection and improper surgical technique.

Rogers and Morris (1967) reported on a percutaneous lead

\[^1\]E. I. du Pont de Nemours and Company, Wilmington, Delaware.
system for power and control of artificial hearts. Two models of molded silicone patches faced with dacron felt were used. A silastic tube was attached to the center of the patch in such a manner that it could be pulled through at the indicated time. The implantation consisted of a two stage operation. The patch was implanted subcutaneously and after three weeks if it was accepted by the tissues, a skin incision was made over it and the silastic tube was drawn through the center of the patch. Four out of 10 implants of the first model and 6 out of 11 of the second model were rejected.

Gillette (1966) utilized a cartwheel "Transdermor" made of teflon to secure plastic tubes entering the viscera. The implant was well tolerated in six sheep and five dogs and was functional for two months when the investigation was terminated.

Prosthetic Materials

Numerous varieties of metals and synthetics have been used as prosthetic agents to replace portions of malformed or diseased organs and tissues. Metals are used in orthopedic surgery for the correction of fractures and the re-establishment of joints. Synthetics have been used to replace deformed subcutaneous tissues and bones in cosmetic and reconstructive surgery. Blood vessels, heart valves, ureters and bile ducts have been successfully replaced by
Materials used as prosthetics should meet the standards defined by Scales (1953):

1. Not physically modified by soft tissue.
2. Chemically inert.
3. Not causing foreign body reactions or inflammation.
5. Non-antigenic.
6. Resistant to mechanical restraints.
7. Fabricable in desired forms.
8. Sterilizable.

Freeman et al. (1965) added two more properties to this list:

9. Resemble the surrounding tissue in consistency without joints or seams.
10. Rigid in both fixation and position.

Some of the synthetic polymers which have been used in medicine are: silicones, teflon, dacron, ivalon, orlon, nylon, marlex\(^1\), polyvinyl chloride, and polyethylene. The medical uses and host reactions of silicones and teflon are well documented in the literature and they fulfill most of

the properties established for acceptable prosthetics.

Silicone

The medical grade silicone compounds are polymers of dimethyl siloxane. According to Blocksma and Braley (1965), silicones are composed chemically of long chains of alternating silicone and oxygen atoms. Usually methyl or phenyl groups are attached to the silicone atom. The structure of silicones is projected as:

\[
\begin{array}{c}
R \\
\downarrow \\
Si - O - Si - O \\
\downarrow \\
R \\
\end{array}
\]

"R" can be any organic group.

Brown _et al._ (1960) reported that the viscosity of silicones is determined by the length of dimethyl siloxane chains. Fillers and vulcanizing agents are compounded with the base polymer for various forms of silicones. The medical grade silicone rubber is made of high viscosity silicone polymers. Benzoyl peroxide is used to detach a hydrogen from a methyl group and form cross linkage to change its resinous state to a pliable or solid form.

Silicones are commonly used in cardiovascular surgery. Daggett and Austen (1967) reviewed their uses in heart valves, extracorporeal circulation, membrane oxygenators, vascular cannulas, thoracostomy tubes, implantable cardiac pacemakers...
and carriers for prolonged drug release. Silicone rubber tubing and valves are used in neurosurgery as ventriculo-atrial shunts in hydrocephalic conditions.

In nasal reconstructive surgery silastic was used by Beekhuis (1964) in 16 patients, where 23 implants were well tolerated for periods up to 15 months. The author was very optimistic about the use of silicone rubber in reconstructive surgery. To achieve satisfactory results proper sterilization of the implants, aseptic techniques and correct surgical methods were recommended.

Lipshutz (1966) evaluated subdermal and subcutical silicone implants in 71 patients. Various blocks, sheeting, sponges, and breast prostheses made of silicone rubber were implanted for cosmetic reasons. Twelve percent of the 88 implants had to be removed because of errors in judgement or technique.

Silicones have been used in opthalmic surgery as corneal implants by Brown and Dohlman (1965). Liquid silicone has been employed as a substitute for vitreous humor in cases of detached retina, Stone et al. (1965).

Folkman and Long (1964) utilized silicone rubber as a carrier for prolonged drug therapy. Digitoxin, triiodothyronine, tyrosine, sodium ethylenediamine tetra-acetic acid (EDTA), isoproterenol and thyroid $^{125}$I were incorporated into silastic capsules. These capsules were implanted into
the cardiac muscle of dogs where previously heart blocks were 
induced. Satisfactory results were achieved in overcoming 
heart block in these animals. The capsules were surrounded 
by a fibrous tissue in the myocardium which could be a 
limiting factor in release of the medication. Other medi­
cines could be incorporated into silicone rubber and implanted 
subcutaneously or intra-peritoneally where less fibrosis would 
occur providing a more prolonged release of drugs.

Egdahl (1955) reported unsatisfactory results on the use 
of silicone rubber for aortic grafts. He implanted 2.5 cm 
of silicone rubber in segments of the abdominal aorta of ten 
dogs. Only two grafts remained patent during post-operative 
recovery.

Harris and Carleton (1966) investigated the use of room 
temperature vulcanizing silicone rubber (RTV) for paralytic 
dysphonia and compared its histological response to that of 
teflon. The reaction to silicone consisted of fibrosis with 
a zone of chronic inflammatory cells surrounding the silicone. 
A mixture of glycerine and teflon injected into the vocal 
cords resulted in foreign body giant cells engulfing the 
teflon particle. They concluded that RTV silastic was 
superior to teflon paste for augmentation procedures.

Silicone rubber tubing has been used as a portion of 
lead systems by Cholvin (1961), Rogers and Morris (1967), 
Lillehei et al. (1967), and many others. Tissue reactions
In comparison to other polymers are considered minimal. Freeman et al. (1965) have claimed that injections of dimethylpolysiloxane fluid into the skin and subcutaneous tissue of mice have not produced gross or microscopic inflammatory responses. The residual silicone liquid was encapsulated by a thin membrane with only a small loss of the injected fluid. They also injected RTV Silastic S-5392 in dogs and a mixture of this and liquid silicone in mice. A thin membrane free of fibrosis or inflammatory reaction encapsulated the silicones. They concluded that injected silicones were totally inert and elicited no inflammatory or reparative reaction in subcutaneous tissues.

Rubin (1966) injected liquid silicone and RTV silastic into the vocal cords of dogs. Mononuclear cells surrounded the liquid silicone for a period not exceeding one week. Absorption of the fluid occurred after several months. There was no tissue reaction to RTV silastic and the histologic appearance at the sixth post-operative day was identical to that at six months.

Agnew et al. (1962) evaluated silicone rubber for surgical prostheses. The prosthetic material was implanted into the cerebral cortex, peritoneal cavity and abdominal subcutaneous tissue of 50 Wistar rats. There were no significant reactions in the brains. In several of the other tissues, a chronic inflammatory reaction was noticed. The
subcutical and peritoneal implants were encapsulated by a fibrous tissue and occasionally giant cell and histiocytic reactions were seen around the implants. Although three tumors were observed in a 22 month period, none of these were implant related.

The tissue reaction to polymers may vary with the size of the implant, the larger implants frequently causing more reaction. Silicones have been used in cosmetic surgery as augmentation of the breast or facial bones. Winer et al. (1964) reported on three cases of siliconomas, two in the breast and one on the face. The reactions were typical foreign body granulomas. Nosanchuk (1968) reported on a case of silicone granuloma in the breast of a woman who had received silicone injections three years previously.

Marzoni et al. (1959) implanted three forms of silicone rubber into a 2 cm defect in three ribs of seven dogs. No tissue invasion was found in the sponges which were encapsulated by a moderate amount of fibrous tissue. The general tissue reaction was characterized by fibrosis with very few giant cells or mononuclear cell infiltration.

Polytetrafluoroethylene (Teflon)

Teflon is tetrafluorocarbon made by polymerization of tetrafluoroethylene at high temperatures and pressure. Its structure is:
It is a non-wettable material, which is stable from -195 to 325° C, and has a specific gravity of 2.1.

This material has been used extensively in cardiovascular surgery. Daggett and Austen (1967) reviewed the various forms of teflon and its uses in cardiovascular surgery. Woven teflon cloth was used in replacement of the thoracic aorta in aortic aneurysms and coarctations of the aorta. Teflon weaves or knits were used in artificial heart valves and patch closures of intracardiac defects. Teflon was also used in connector cannulas and other components of heart-lung machines and as insulators for electrodes used in cardiac pacing.

Various forms of teflon have been used to replace tissue defects. Harrison (1957) compared tantalum wire gauze, open weave teflon and a close weave teflon to correct both clean and infected defects in the abdominal walls, thoracic walls and diaphragms of 41 dogs. Best results were obtained with the open weave teflon, where ingrowth of fibrous tissue was distinct. The close weave teflon was found to be a complete failure. The open weave teflon was superior to tantalum because of its pliability and longer duration of strength.

Teflon has been used to replace the external acoustic
meatus of dogs. Sis (1963) utilized a teflon tube for this purpose. He recommended its use in hypertrophy, induration, inflammatory polyps, neoplasms and chronic ulcerative lesions of the external acoustic meatus.

Pearson (1962) used a teflon implant to assist in correcting medial patellar luxations in dogs. Cholvin (1961) reported on the use of a teflon skin grommet and insulated wire as a lead system in experimental physiology. Hughes and Lontz (1964a,b) used teflon as an artificial bile duct for correction of biliary obstruction.

Teflon was used in plastic reconstructive surgery. Fedun (1967) reported on its use in 76 operations in deformed noses. Teflon mesh was implanted under the cutaneous muscles of the nose of rabbits and they were observed for periods of 7 days to 18 months. Histological changes at the end of the seven days consisted of accumulation of fibroblasts, histocytes and leucocytes at the implantation site. Argyrophilic reticular fibers were present near the implant. The regenerated acid mucopolysaccharide ground substance, which reacted with colloidal iron, disappeared after application of a bacterial hyaluronidase. This proved the presence of hyaluronic acid in the regenerating tissue surrounding the implanted teflon. By two weeks, soft granulation tissue surrounded the implant and filled the opening of the mesh. Complete coverage of the transplants took 40 to 45 days. At
that time an equilibrium of the mucopolysaccharide complex became evident. Even after three to four months, the granulation was not complete. Neutral mucopolysaccharides were prevailing in 18 month granulation tissue. No anaplastic changes were noticed in the fibers.

The reconstruction of the thoracic trachea was attempted in dogs by Aletras et al. (1964), where 6 to 9 tracheal rings were removed. Teflon or silastic tubes were implanted to serve as inner tubes. A pericardial pedicle flap was used as an outer layer and ivalon rings were sutured over the pedicle. The silastic tubes had a tendency to become displaced and the teflon tubes could not be removed. Teflon rings were used with teflon and silastic tubes in two additional groups of dogs. Granulation tissue protruded into the lumen, and a foreign body reaction was evident around the sutures and prosthetic materials. Profuse proliferation of fibrocartilage was observed in the vicinity of the implants. Epithelial regeneration was present in a few cases with mostly endothelial like cells on the surface of the sclerotic connective tissue. Minimal inflammatory reactions were reported.

Tissue Reactions to Silicone and Teflon

Most of the polymers have not fulfilled the standards set by Scales (1953). Physiologic incompatibility and carcinogenesis were the most limiting factors in their use as prosthetic materials. Oppenheimer et al. (1955) reported
on implant related tumors. Twenty-nine of 13 types of
plastics were embedded into rats. Of the 275 tumors, 85
percent were fibrosarcomas, osteogenic sarcomas and
rhabdomyosarcomas.

Silastic sheets 0.25 cm thick were embedded in 35 rats
which survived the minimum latent period of six months.
Malignant tumors were reported in 40 percent of the animals.
The tumor incidence as a response to 0.02 cm plain teflon
film was 23.5 percent of 34 rats. Perforated film teflon
showed 18.7 percent of 32 rats having implant related tumors.

Oppenheimer et al. (1958) working on the same subject,
claimed that removal of the abdominal embedded plastics and
their encapsulating membrane from the rats within a six
month period prevented tumor formation, but removal at a
later time did not prevent neoplastic developments. Sometimes
tumors appeared several months after the films were removed.

Long term studies of tissue effects of certain polymers
in the abdominal subcutis of rats were conducted by Russell
et al. (1959). Glass, polyvinyl alcohol sponge, regenerated
cellulose film, five varieties of silastic and teflon film
were imbedded in the abdominal wall of Wistar rats. No
metastasis was reported in four spindle cell sarcomas and
one undifferentiated sarcoma found in 299 rats observed for
300 days. Different varieties of silicone rubber were
implanted into a group of rats and in those surviving more
than 300 days, only one animal developed a sarcoma at 562 days. Sarcomas were reported in 2 of 55 rats surviving more than 300 days. Sarcomas developed 659 days after implantation of teflon film. In this study there was an incidence of 1.7 percent malignant tumors. Smaller implants with smaller total uninterrupted plane-surface area resulted in a lower tumor incidence.

Little and Parkhouse (1962) reported on the tissue reactions to polymers. Four uniform discs of various polymers 1 mm thick were implanted in the subcutis of guinea pigs. The animals were killed at the end of six weeks, the tissues surrounding each implant were excised and examined histologically. X-ray diffraction was also utilized to study the polymers after implantation. There was a direct correlation between the size of the polymers and the extent of the fibroblastic reactions. The reaction was partially caused by mechanical friction with the surrounding tissues.

Some of the plastics change their properties after implantation. Leininger (1965) reviewed the literature in this regard and reported that dacron and silastic produced the least change in periods up to 18 months. LeVeen and Barberio (1949) emphasized the importance of physico-chemical properties of materials on tissue reactions. Non-wettable materials produced the least tissue reaction.
MATERIALS AND METHODS

The Lead System

The lead system was composed of two portions: an intercostal piece which was made of polytetrafluoroethylene (teflon) and a silicone rubber tubing portion (silastic).

The intrathoracic percutaneous lead system was designed structurally to provide stability between the ribs and to serve as a protective conduit for the silastic tubes. For descriptive purposes, the intercostal teflon piece had the appearance of a "cartwheel". The intercostal piece will be heretofore referred to as the conduit. The diameter of the circular frame was 40 mm, and was connected by four spokes to a hub which had an inner diameter of 10 mm. The thickness of the frame, hub and spokes was 2 mm. The hub extended 10 mm on the thoracic side and ended in a circumscribed lip of 3 mm, which when placed under the ribs, provided stability to the device. The external side of the hub was 18 mm long. This external portion was threaded and a washer was positioned on the hub to protect the skin site from mutilation and contamination. The washer was made of teflon with a thickness of 2 mm and a diameter of 40 mm (Figures 1 and 2).

A silicone rubber tube with a 10 mm outer diameter and an inside diameter of 6.2 mm was introduced through the hub to a distance 50 mm beyond the intrathoracic edge, and 10-20 mm beyond the cutaneous edge.
Figure 1. A. The teflon intercostal piece of the thoracic percutaneous lead. The lip of the conduit is seen on the left and the threated portion of the hub on the right.

Figure 1. B. The protecting washer is to the right of the conduit.

Figure 2. The thoracic percutaneous lead system assembled. The silastic tube is passed through the hub of the teflon conduit.

A. Intrathoracic silastic tube

B. Intracostal portion of the hub

C. Subcutaneous and cutaneous portion of the hub

D. The external silastic tubes
The silastic tube was bonded to the teflon hub by pre-etching the latter surface with peroxide etching agent\textsuperscript{1} for 10-15 sec. The teflon conduit was then dropped into a detergent solution and brushed generously to remove the Tetra-Etch from the inner surface of the teflon hub. Following this, the teflon was placed in naptha for 15 minutes to remove any oils or detergent, and then rinsed in distilled water and air dried.

The inner surface of the teflon hub, was covered with a layer of silicone adhesive.\textsuperscript{2} The silicone rubber tube was introduced into the hub for the desired length.

Several silastic tubes of smaller diameter could be passed through the silicone rubber tube according to the need for monitoring or control purposes. The interthoracic end of the silicone rubber tube was sealed with silastic medical adhesive. The device was allowed to bond for eight hours. It was sterilized in aqueous benzalkonium chloride,\textsuperscript{3} 1:750 solution, for 24 hours prior to use.

\textsuperscript{1}Tetra-Etch, W. L. Gore and Associates, Inc., Newark, Delaware.

\textsuperscript{2}Silastic Medical Adhesive grade A., Dow Corning, Midland, Michigan.

\textsuperscript{3}Zephiran chloride, Winthrop Laboratories, Inc., 90 Park Avenue, New York, New York.
Experimental Animals

Twenty-four medium sized mongrel dogs were selected regardless of age or sex. A pre-surgical examination was performed to determine their health status. All dogs were vaccinated for canine distemper and treated when indicated for internal parasites. The long haired dogs were clipped and all animals were dipped in an insecticide a few days prior to surgery. Animals were kept in cages in a well ventilated room. Cages were cleaned daily and a standard dry dog food was fed ad lib.

The 24 dogs were divided into four equal groups. Group one was observed 30 postoperative days; the second group for 90 days; group three for 210 days; and the fourth group for 365 days. After these intervals, each animal was anesthetized with pentobarbital sodium and photographs of the cutaneous leads were taken. The skin in the vicinity of the lead and implant was swabbed for bacteriological examinations. A venous blood sample was taken for hematological examinations. Euthanasia was performed with an overdosage of pentobarbital sodium and necropsies were performed immediately. Swabs of the thoracic portion of the silastic tube were cultured for bacteria. Fresh representative tissue specimens were saved for histopathology in 10 percent buffered formalin and after 48 hours fixation, bones were decalcified in Decal.\(^1\) Tissues were embedded

\(^1\) Decal, Omega Chemicals, Cold Springs on Hudson, New York
in paraffin, cut sections were stained with hematoxylin and
eosin, and some sections were stained with Gomori's
trichrome stain as described by the Armed Forces Institute
of Pathology (1960).

Anesthesia and Presurgical Preparations

All dogs were given 0.6-1.2 mg atropine sulfate sub-
cutaneously. Anesthesia was induced by intravenous injection
of 4 percent thiamylal sodium\(^1\) at a rate not exceeding 18
mg/kg of body weight. The trachea was intubated with an
endotracheal catheter. A surgical level of anesthesia was
maintained with methoxyflurane\(^2\) in a closed circle system.
An automatic respirator\(^3\) was used when the pleural cavity
was exposed.

The left thoraco-abdominal region was clipped with a
\#40 clipper blade. The surgical field was scrubbed three
times with a surgical soap, flushed with water, dried and
tincture of benzalkonium chloride\(^4\) was applied. The surgical
field was draped with sterile cloth drapes, leaving a suffi-
cient opening to expose the operative field. Aseptic tech-

---

\(^1\)Surital, Park-Davis, & Co., Detroit, Michigan.

\(^2\)Metofane, Pitman-Moore, Indianapolis, Indiana.

\(^3\)Bennett Assistor Model BA-2, Bennett Respiration
Products, Inc., Los Angeles, California.

\(^4\)Tincture Zephiran, Winthrop Laboratories, Inc., 90 Park
Ave., New York, New York.
techniques were practiced during the entire surgical operation.

Surgical Anatomy and Technique

A five centimeter skin incision was made on the upper third of the fourth intercostal space, caudal to the posterior edge of the scapula. The cutaneous trunci muscle was incised and separated from serratus ventralis muscle. The skin and cutaneous trunci muscles were retracted caudally to expose the intercostalis externus muscle, which was incised along with the intercostalis internus muscle and the pleura to expose the pleural cavity.

At this stage, artificial respiration was started. The incision in the intercostal muscles was extended for five centimeters. Medium weight synthetic\(^1\) sutures were passed around the 6th and 7th ribs. The implant was rinsed with normal saline, to remove the benzalkonium chloride solution used for chemical sterilization. The implant was introduced between the ribs and the silastic tube was placed between the cardiac and diaphragmatic lobes of the lung. The tip of the tube was contacting the pericardium. The lip to the hub was placed under the ribs on the thoracic side. Slight traction was applied to the implant to ascertain its stability. The sutures were threaded through the openings of the teflon wheel and ligated to provide additional

\(^1\) Vetafil Bengen, Bengen and Co., Hannover, West Germany.
stability.

The serratus ventralis muscle was sutured around the hub with catgut sutures. A hole was made with a 5 mm cork borer 20 mm posterior to the original skin incision. The hole was made smaller than the size of the hub to provide a tight seal. The external portion of the silastic tube and the threaded portions of the conduit were passed through the skin opening. Three sutures were placed around the spokes and the serratus ventralis muscle. The skin was attached to the muscle with three additional sutures. A continuous subcutical stitch was used to bring the edges of the wound into close approximation. The skin incision was closed with interrupted dermal sutures.

An antibiotic wound powder\(^1\) was applied to the skin incision around the implant. The teflon washer was applied to its threaded external portion. Air was aspirated from the pleural cavity until negative pressure was achieved.

The post-operative care consisted of daily application of the antibiotic wound powder for two weeks. Systemic antibiotics were given only when indicated.

\(^{1}\) Keraspray, E. E. Massengill Co., Veterinary Division, Bristol, Tennessee.
RESULTS

Group 1: 30 Days Observation Period

This group of dogs had no complications for 30 days following surgery. The implants were well tolerated and no exudate was present at the junction of the implants and skin (Figure 3).

Macroscopic lesions

The threads of the conduit in the subcutical region were filled in with granulation tissue. The lips of the conduit between the sixth and seventh ribs were covered by a layer of granulation tissue at the pleural surface. The cardiac and diaphragmatic lobes of the left lung were adhered and covered by a thick layer of granulation tissue. In all dogs both lobes were adhered to each other around the silastic tubes. These consisted of 2-3 mm thick adhesions that had surrounded the tubes and formed cul-de-sacs (Figures 7 to 9). The pleura at the edges of the sacs was 2-3 mm thick and gradually decreased in thickness towards the periphery. In one dog, the lungs were slightly adhered to the entrance site of the silastic tube into the thoracic cavity. There was mild congestion and ecchymosis in the mediastinum adjacent to the tube.

The ribs were two to three times thicker around the conduit, and a semilunar bony groove was formed by proliferated...
Figures 3-6. The external appearance of the thoracic percutaneous lead system at the end of each observation period

Figure 3. Upper left dog #683, 30 days

Figure 4. Upper right dog #674, 90 days

Figure 5. Lower left dog #660, 210 days

Figure 6. Lower right dog #668, 365 days
Figure 7. Upper left dog #685, 30 days. Adhesions of left lung to thorax adjacent to lead system

Figure 8. Upper right dog #685, 30 days. Note adhesion tags and granulation tissue surrounding lead system after forcibly removing left lung

Figure 9. Lower left dog #680, 30 days. The cardiac and diaphragmatic lobes of the left lung have adhered to each other and formed a cul-de-sac around the silastic tube

Figure 10. Lower right dog #673, 90 days. Note the marked thickness of the sixth and seventh ribs, and groove around the lip of the conduit on the intercostal surface of both ribs
tion of new bone around the hub of the teflon conduit. There were no other obvious lesions in the thoracic or abdominal organs.

**Microscopic lesions**

The skin and subcutis around the conduit showed minimal tissue reaction. The threads of the conduit hubs were filled with mature collagenous tissue (Figures 11 to 14). A few plasma cells were found intermingled between the collagen fibers at the superficial borders of the implants but were absent in the deeper zones of muscular tissue (Figures 15 and 16).

There was evidence of infection in one dog, #685, which did have collagenous fibrous tissue filling the space between the threads of the conduit, with a lack of inflammatory cells in some areas, however, there was some inflammatory reaction in other areas. The inflammatory reaction was characterized by an infiltration of neutrophils, plasma cells, histiocytes and proliferation of capillaries. The inflammatory zone was encapsulated by a zone of fibrous connective tissue in which moderate numbers of plasma cells were present. There was slight evidence of degeneration in muscle fibers adjacent to the conduit hubs and the muscles were replaced with fibrous connective tissue.

In all six dogs, the ribs had considerable amounts of periosteal new bone formation around the sites of contact.
Figure 11. Upper left dog #684, 30 days. Tissue growth into the threads of the conduit hub in the subcutis. X 14

A. Space occupied by teflon
B. Tissue growth into the threads

Figure 12. Upper right. Higher magnification of Figure 11 at B. Note absence of inflammatory reaction. X 114

Figure 13. Lower left dog #680, 30 days. Tissue growth into threads of conduit in the subcutis. No inflammatory reaction was seen. X 56

Figure 14. Lower right dog #681, 30 days. Tissue reaction around the conduit threads. Numerous plasma cells scattered between collagen fibers. X 56
Figure 15. Upper left dog #681, 30 days. Reaction around the hub of the conduit in the subcutis. X 114

A. Mature granulation tissue
B. Plasma cells and histiocyte infiltration

Figure 16. Upper right. Higher magnification of Figure 15. X 140

Figure 17. Lower left dog #680, 30 days. Reaction of the tissues around the conduit. Gomori's trichome stain. X 14

A. Granulation tissue covering the contact surface between the rib and the conduit
B. Islands of proliferating cartilage
C. Endochondral ossification
D. Periosteal new bone
E. Original part of the rib

Figure 18. Lower right. Higher magnification of Figure 17. Gomori's trichrome stain. X 56

A. Proliferating cartilage cells
B. Endochondral ossification
C. Fibrous periosteum
with the conduit hubs. Collagenous fibrous tissue 1-2 mm thick covered this contact surface. Periosteal new bone formation at the contact sites had developed in an eccentric pattern around the conduit hubs and into the intercostal spaces. The new bone formations were considerably thicker on the lateral sides of the ribs than on the medial sides, sometimes increasing to almost twice the thickness of a normal rib. These proliferations were characterized by peripheral periosteal hyperplasia underlined with a thick layer of chondroblasts and chondrocytes which were gradually replaced with osteoid tissue and trabecular formation in the deeper zones (Figures 17 and 18).

The pleural surfaces of the ribs around the lip of the conduit hubs contained thick mature granulation tissue in all dogs. The granulation tissue was about 3 mm thick at the conduit junction decreasing gradually towards the periphery. There were no anaplastic changes in the fibrocytes in the granulation tissue. In one dog, #685, the granulation tissue was infiltrated with neutrophils, plasma cells and histiocytes. The scar tissue formed around the lungs in all dogs had histological similarities. Both cardiac and diaphragmatic lobes were adhered to each other and enclosed the silastic tubes. The adhesion sites were composed of zones of granulation tissue which were about 2-3 mm thick, decreasing gradually away from the silastic tubes.
The cul-de-sacs, which were formed in the interlobular spaces around the silastic tubes, consisted of a thin zone of a few cells of immature fibroblasts surrounded by mature granulation tissue 2-3 mm in thickness. The pleurae were continuous with the granulation tissue. There was slight atelectasis in a 2-3 mm thick zone of the lungs in areas adjacent to the adhered lobes (Figures 19 to 22).

Occasional plasma cells and neutrophils were scattered throughout the granulation tissue. In one dog, #685, the mediastinal pleura and a focal area of pericardium had neutrophils and plasma cell infiltrations respectively. There were no histological lesions in the remaining thoracic and abdominal viscera.

Bacteriological examination of Group 1

During the second post operative week, swabs of the skin and prosthetic junction sites were collected and cultured for bacteria. *Staphylococcus aureus* was isolated from two of six dogs. At necropsy only one of these dogs, #685, had *Staphylococcus aureus* in the cultures of the same area. *Staphylococcus aureus* was also cultured from the intrathoracic portion of the silastic tube in this dog.

*Echerichia coli* was isolated from the conduit-skin junction of dog #684. Two weeks later, at the time of necropsy, cultures of the same area failed to reveal pathogenic bacteria in five dogs (see Table 1).
Figure 19. Upper left dog #683, 30 days. Site of intra-lobular adhesion. X 56

A. Alveolar space
B. Thickened pleurae
C. Immature granulation tissue

Figure 20. Upper right dog #682, 30 days. Cul-de-sac formed around the silastic tube by the lung. X 56

A. Alveolar space
B. Atelectatic zone infiltrated with plasma cells, histiocytes and fibroblasts
C. Mature granulation tissue

Figure 21. Lower left dog #683, 30 days. Adhesion site between the diaphragmatic and cardiac lobes. X 56

A. Cardiac lobe
B. Immature granulation tissue
C. Diaphragmatic lobe

Figure 22. Lower right dog #685, 30 days. Cul-de-sac formed around silastic tube by the lungs. X 56

A. Atelectatic zone in the lung
B. Pleurae
C. Mature granulation tissue
<table>
<thead>
<tr>
<th>Observation period (days)</th>
<th>Dog No.</th>
<th>Staphylococcus aureus</th>
<th>Proteus vulgaris</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>680</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>681</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>682</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>683</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>684</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>685</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>3224</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>662</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>663</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>673</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>674</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>675</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td>210</td>
<td>659</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>660</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>661</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>669</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>670</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>672</td>
<td>+ +</td>
<td></td>
</tr>
<tr>
<td>365</td>
<td>664</td>
<td>+</td>
<td>+ +</td>
</tr>
<tr>
<td></td>
<td>665</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>666</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>667</td>
<td>+</td>
<td>+ +</td>
</tr>
<tr>
<td></td>
<td>668</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td></td>
<td>671</td>
<td>+ + +</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>24</td>
<td>10 8 4</td>
<td>4 4 2</td>
</tr>
</tbody>
</table>

*a*First column: midtrial culture of the superficial area of conduit-skin junction;  
Second column: culture of above area at necropsy;  
Third column: culture of the silastic tube at the intra-thoracic site.
<table>
<thead>
<tr>
<th>Streptococcus canis</th>
<th>Pasteurella multocida</th>
<th>Escherichia coli</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>1 2 2</td>
<td>1 1</td>
<td>2</td>
</tr>
</tbody>
</table>
Group 2: 90 Days Observation Period

This group tolerated the lead system except for two dogs, #663 and #675. An erythematous zone appeared in the skin over the ventral aspect of the conduit two months after surgery in dog #663. This area gradually became thinner and in seven days a portion of the conduit started to extrude through the skin. After 30 days, about 4 cm of rim and two of the spokes were visible. Although the conduit was extruding through the skin there was no significant quantity of exudate at the conduit-skin junction. Surgical reposi­tion­ing of the extruded portion of the lead system was not attempted (Figure 23A).

Dog #675 developed a fistulous tract at the ventro-lateral aspect of the lead system 60 days after surgery. There was a purulent discharge from the fistulous tract and also from the periphery of the conduit-skin junction.

Macroscopic lesions

At necropsy the gross changes in the skin, subcutaneous tissues, ribs and lungs were identical in four animals (Figure 4). Dog #675 had a fistulous tract 10 cm long, dis­charging at the ventro-lateral aspect of the left thoracic region.

Dog #663 had the ventral portion of the conduit extruding through the skin. The skin and subcutaneous tissues were growing into the threads of the conduit in all dogs. This
Figure 23A. Upper left dog #663, 90 days. Extrusion of the conduit through the skin

Figure 23B. Upper right dog #662, 90 days. The sixth and the seventh ribs. Note the thickened zone of granulation tissue surrounding the orifice of the lead system into the pleural cavity

Figure 24A. Lower left dog #670, 210 days. Extrusion of the ventral portion of the rim of the conduit through the skin

Figure 24B. Lower right dog #671, 365 days. Two fistulous tracts on the lateral aspect of left thoracic wall, above and below the marker
resembled the general appearance of the same area in the 30 day group of dogs.

The ribs at the site of contact with the conduit were tripled in thickness and a 2-3 mm thick granulation tissue surrounded the conduit (Figure 23B). There was a groove in the thickened ribs formed around the lips of the conduit (Figure 10). There was also new bone formation around the granulation tissue surrounding the conduit. A fracture was noticed in the sixth rib of dog #674.

The cardiac and diaphragmatic lobes of the lung were adhered to each other and to the ribs around the intrathoracic portion of the lead system. There were no other gross changes in the lungs. The bronchial lymph nodes in two dogs, #662 and #675, were enlarged. One of these dogs had a *Dirofilaria immitis* infection and the other had an enlarged thymus gland. *Dirofilaria immitis* were found in the right ventricle and pulmonary arteries.

**Microscopic lesions**

The skin and subcutaneous region around the threaded portion of the conduit were about 2-3 mm thick and were composed of mature collagen fibers. The fibrous tissue was molded into the threads of the conduit similar to that of the dogs in the 30 day observation period. A few histiocytes and plasma cells were found intermingled between the collagen fibers (Figures 27 to 30). In two dogs, #663 and
Figure 25. Upper left dog #662, 90 days. Tissue reaction around the threaded portion of the conduit in the subcutis. X 56

A. Mature granulation tissue with few plasma cells between the fibrocytes

B. Space occupied by the conduit

Figure 26. Upper right dog #673, 90 days. Tissue reaction around the teflon hub. X 56

A. Zone of fibroblasts and plasma cells

B. Mature collagen fibers

Figure 27. Lower left dog #662, 90 days. Tissue reaction around the threaded portion of the hub of the conduit in the subcutis. Histiocytes and plasma cells are numerous at the surface. X 56

Figure 28: Lower right. Higher magnification of Figure 26. X 114
There were moderate numbers of neutrophils, eosinophils, plasma cells, histiocytes and proliferation of capillaries on the surface of mature collagenous tissue.

The surfaces of the ribs which had direct contact with the conduit were covered by granulation tissue in which a few plasma cells and histiocytes were present. There were periosteal new bone formations proliferating from the peripheral margins of the contact areas of the ribs towards the intercostal spaces (Figures 29, 31 and 32). These were similar to what was observed in the ribs of dogs in the 30 day observation period. The ribs were considerably thickened and mature osseous tissue had formed around the conduit. There was no osteomyelitis in this group of dogs. In some dogs there were focal areas of consolidated necrotic debris filling the space between the spicules in both the shaft of the rib and the new bone (Figure 33). The fracture seen in the sixth rib of dog #674 was characterized by a central hematocyst surrounded by a callus (Figure 30).

The zones of adhesions of the lung to the thoracic wall and around the conduit lips were composed of fibrous connective tissue 2-3 mm thick. The cul-de-sac formed around the silastic tube was covered on the luminal surface by an epithelial layer. This layer consisted of ciliated columnar and cuboidal cells undergoing hypertrophic and hyperplastic changes. There were areas of squamous metaplasia in the
Figure 29. Upper left dog #663, 90 days. Reaction between the conduit and the rib. X 56

A. Mature granulation tissue
B. Periosteal new bone formation

Figure 30. Upper right dog #674, 90 days. Fracture site of the sixth rib. X 54

A. Bone
B. Callus
C. Endosteal hematocyst

Figure 31. Lower left dog #674, 90 days. Periosteal new bone formation in seventh rib at the contact surface with the conduit. X 56

A. Space occupied by the conduit
B. Granulation tissue
C. Periosteal hyperplasia

Figure 32. Lower right dog #674, 90 days. Reaction of the rib around the conduit. X 56

A. Space occupied by the conduit
B. Granulation tissue
C. Mature collagen fibers
D. Bone
Figure 33. Dog #662, 90 days. Consolidated necrotic debris between the spicules of the new bone formed around the teflon conduit. X 56

Figure 34. Dog #672, 210 days. Pseudoarthrosis and osteoclasia in the sixth rib. Note osteoclasts on the surface of the bone and the mature collagen fibers on the contact surface with the conduit. X 56
epithelial zone. The subepithelial layer was composed of mature granulation tissue 3-4 mm thick. Plasma cells and histiocytes were sparsely scattered among the collagen fibers (Figures 35 to 40).

Some atelectasis, plasma cells, histiocytes and neutrophils were present in the lung surrounding the fibrotic sac. The zone of atelectasis was 2-3 mm thick.

In two dogs, numerous neutrophils, histiocytes, and plasma cells had infiltrated into the fibrous connective tissue. The bronchial lymph nodes were infiltrated with moderate numbers of neutrophils and histiocytes. The sinusoids were edematous and filled with a proteinaceous fluid.

Bacteriological examination of Group 2

The midtrial cultures of the conduit-skin junction revealed *Staphylococcus aureus* in three dogs and *Escherichia coli* in one dog. Dog #675 developed a fistulous tract two months after surgery. *Staphylococcus aureus* was isolated from the discharge and it was treated with a penicillin-dihydrostreptomycin combination for one week, at a rate of 1 ml/5 kg of body weight intramuscularly.

At necropsy *Staphylococcus aureus* was cultured from the conduit-skin site of four dogs (#663, #673, #674, and

---

Figure 35. Upper left dog #662, 90 days. Reaction of the lung around the silastic tube. X 114

A. Epithelial hyperplasia and squamous metaplasia

B. Granulation tissue

Figure 36. Upper right. Lower magnification of Figure 35. Note the extent of granulation tissue in the subepithelial zone. X 56

A. Epithelial hyperplasia and squamous metaplasia

B. Mature granulation tissue

Figure 37. Lower left dog #663, 90 days. Reaction of the left lung around the silastic tube. X 114

A. Neutrophils and plasma cells in the lumen of the cul-de-sac

B. Hypertrophy and hyperplasia of columnar epithelium

C. Subepithelial granulation tissue

Figure 38. Lower right dog #673, 90 days. Acute inflammatory reaction in the lumenal surface of the cul-de-sac formed around the silastic tube. X 56

A. Loose piece of silastic

B. Neutrophils, histiocytes and plasma cells

C. Mature collagen fibers
Two of these dogs, #663 and #673, harbored the same organisms in the intrathoracic portion of the lead system. *Streptococcus canis* was also isolated from the same intrathoracic portion of the lead system from dog #663 (Table 1).

**Group 3: 210 Days Observation Period**

Four dogs (#659, #660, #669, and #672) tolerated the lead system during the observation period without obvious complications (Figure 5). Extrusion of the dorsal portion of the conduit rim occurred in the sixth post operative month in two dogs, #670 and #661. Approximately 1 cm of the conduit extruded through the skin. There was minimal discharge around the skin site of the lead system in these two dogs (Figure 23).

**Macroscopic lesions**

The gross changes at the time of necropsy consisted of proliferation of granulation tissue around the threads of the conduit in the subcutaneous region. Granulation tissue also formed around the spokes and the rim of the conduit wheel, but it was less extensive than around the hub.

There was thickening of the ribs and periosteal new bone formation surrounding the hub of the conduit in four dogs. These changes were similar to the changes in the previous two groups. In dog #670 the conduit had formed an angle with the rib cage so that the sixth rib was in contact
Figure 39. Upper left dog #663, 90 days. Reaction of the lung around the silastic tube. Note epithelial hypertrophy and hyperplasia on the surface and proliferation of fibrous connective tissue in the subepithelial zone. Gomori's trichrome stain. X 56

Figure 40. Upper right dog #663, 90 days. Reaction of the lung around the silastic tube. Note epithelial hypertrophy and hyperplasia and presence of a few mitotic figures. X 140

Figure 41. Lower left dog #660, 210 days. Reaction of the lung around the silastic tube. Note squamous metaplasia on the lumenal surface of the cul-de-sac. X 56

Figure 42. Lower right. Higher magnification of Figure 41. X 140
with the conduit of the lead system while the seventh rib was not contacting the conduit. A 2.5 cm long osseous channel formed around the conduit in the sixth rib. The new proliferating osseous tissue was wider at the dorsocaudal aspect of the rib and it was funneled dorsocranially.

In dog #672 the portion of the sixth rib contacting the conduit was completely lysed and formed a pseudarthrosis; there was a 1.5 cm defect in the rib at this site. A fracture was seen in the seventh rib at the contact site. Circumferential new bone formation and thickening of the rib around the conduit was evident.

The lungs were adhered around the lips of the conduit and formed a cul-de-sac around the silastic tube. No gross changes were observed in the lungs or thoracic viscera other than the adhesion of the lung to the site of original surgical incision in the sixth intercostal space.

In one dog (#659) the lungs were not adhered to the incision line or around the lip of the conduit. The pleural surface of the left lung was covered by a thick layer of granulation tissue at the site of friction with the silastic tube.

Microscopic lesions

Histological changes in the skin and subcutaneous tissue were characterized by formation of collagenous tissue 2-3 mm in thickness around the threaded portion of the conduit.
Plasma cells, histiocytes, and occasionally neutrophils were found between the collagen fibers at the contact surface (Figures 43 to 45). In three of the dogs there was a thin loosely arranged membrane covering the contact surface. The membrane was composed of proliferating capillaries surrounded by neutrophils, plasma cells, histiocytes and occasionally fibrocytes. The deeper zones in the subcutis area had more collagen fibers and less inflammatory cells. The collagen fibers surrounding the conduit rim or spokes were considerably thinner and inflammatory cells were very sparse. Neutrophils, plasma cells and histiocytes were seen on the surface of granulation tissue surrounding the conduit in dog #672. This was forming a fistulous tract in the subcutaneous region (Figure 46).

The histological changes in the ribs were similar to those in Groups 1 and 2. Periosteal new bone formation was proliferating in an eccentric pattern around the rib. The ribs were two to three times thicker than a normal rib. The area of contact between the ribs and conduit was covered by a thick layer of fibrous connective tissue in which a few plasma cells and histiocytes were scattered among the fibrocytes (Figures 44, 49 and 50). Osteoclasia was evident on the surface of the rib contacting the conduit in some of the dogs. There were also islands of endochondral ossification scattered at the margins of the periosteal new bone.
Figure 43. Upper left dog #669, 210 days. Tissue reaction to conduit in the subcutis. X 56

A. Fibroblasts and plasma cells
B. Mature collagen fibers

Figure 44. Upper right. Higher magnification of Figure 43. Note plasma cells between collagen fibers. X 140

Figure 45. Lower left dog #670, 210 days. Focal accumulation of plasma cells among collagen fibers. X 350

A. Plasma cells
B. Collagen fibers

Figure 46. Lower right dog #672, 210 days. Reaction around the fistulous tract. Profuse infiltration with neutrophils cells, histiocytes, and plasma cells. X 140
Sclerosis of the marrow was observed in this area. Focal areas of consolidated necrotic debris without inflammatory reaction were filling the spaces between the spicules of the ribs and the newly formed bone.

A 1.5 cm defect in the sixth rib of dog #672 was replaced by fibrous connective tissue. This defect was at the site of contact with conduit. The osseous tissue was completely reabsorbed and replaced by mature collagen fibers which were layed down in an annular form (Figure 34). The contact surface was covered by villus proliferation of granulation tissue, and few differentiated mesothelial cells were seen on the surface. Plasma cells were scattered among the collagen fibers. The ends of the reabsorbed bone were characterized by marked numbers of osteoclasts, aligned along the site of reabsorbed bone.

The seventh rib of this dog had considerable numbers of neutrophils, plasma cells, histiocytes and capillary proliferation at the site of contact with conduit. The inflammatory reaction extended through the 3-4 mm thick fibrous connective tissue to the periosteal region of the rib. There was a fracture in this rib which had a distinct central hematocyst gap surrounded by an endosteal callus on both sides (Figure 48).

There was hypertrophy, hyperplasia and squamous metaplasia of the ciliated columnar epithelium on the luminal
Figure 47. Upper left dog #670, 210 days. Tissue reaction between the conduit and rib. X 56

A. Immature granulation tissue infiltration with plasma cells
B. Mature collagen fibers
C. Bone

Figure 48. Upper right dog #672, 210 days. Fracture in the seventh rib. X 14

A. Callus
B. Endosteal hematocyst

Figure 49. Lower left dog #669, 210 days. Tissue reaction between the conduit and rib. X 56

A. Zone of granulation tissue and chronic inflammation
B. Mature collagen fibers
C. Bone

Figure 50. Lower right. Higher magnification of Figure 49 X 140

A. Bone
B. Mature collagen fibers
surface of cul-de-sac formed by the lung around the silastic tube. The subepithelial surface was characterized by accumulation of plasma cells, proliferation of capillaries and fibrous connective tissue. Neutrophils and histiocytes were present in some of the sections in the subepithelial zone of the cul-de-sac. Fibrous connective tissue surrounded the sac and a zone of atelectasis, 2-4 mm thick, was evident in the pulmonary site. Plasma cells, histiocytes, and neutrophils were present in the alveolar space of the atelectatic zone. The alveolar space in some areas was lined by cuboidal epithelial cells. Profuse inflammatory exudate characterized by accumulation of neutrophils, histiocytes and plasma cells were seen in the lumen of the cul-de-sac in dogs #661, #670 and #672.

There were thick adhesions between the diaphragmatic and cardiac lobes of the left lung. Usually the main reaction around the silastic tube involved one lobe of the lung while the adjacent lobe was only slightly involved.

Bacteriological examination of Group 3

 Cultures of the superficial conduit-skin junctions at midtrial revealed Proteus vulgaris in dog #670 and Streptococcus canis in dog #661. Both of these dogs also had Staphylococcus aureus. At the termination of 210 days Proteus vulgaris and Streptococcus canis were isolated from the same dogs and same site, Staphylococcus aureus being
absent. These organisms were not isolated from the deep intrathoracic portion of the lead system.

*Staphylococcus aureus* was isolated from the superficial site of the conduit-skin junction of three dogs at the end of 210 days. One of these dogs, #659, had the same bacteria cultured from the intrathoracic portion of the implant. *Pasteurella multocida* was isolated from both the superficial and intrathoracic portion of the lead system from dog #672 which had a reabsorbed sixth rib and fractured seventh rib. Hence, in this group of dogs, one *Pasteurella multocida* and one *Staphylococcus aureus* infection was evident in the intrathoracic portion of the lead system (Table 1).

**Group 4: 365 Days Observation Period**

Three of the six dogs (#667, #668 and #665) tolerated the lead system during the observation period and no gross complications or purulent discharges from the lead system skin sites were observed (Figures 6, 51 and 52). The other three dogs (#666, #671 and #664) developed bacterial infection around the conduit-skin junctions in the sixth and eighth post operative month. In one of these dogs, #666, the dorsal portion of the rim of the conduit started to protrude through the skin after four months. This occurred gradually and the skin became very thin and erythematous over the teflon rim. Once the conduit started to protrude through the skin, granulation tissue formed around it. No
Figure 51. Dog #667, 365 days. The appearance of the external portion of the thoracic percutaneous lead system at the upper third of the sixth intercostal space.

Figure 52. Close up view of Figure 51
exudate was noticed at this site. Protrusion proceeded until the termination of the experiment when about 3 cm of the rim and one spoke of the conduit extruded through the skin.

Dogs #666 and #671 developed fistulous tracts with a purulent discharge, 10 cm ventrolateral to the lead system site (Figure 24B). The infection in these dogs was noticed the eighth post operative month. These dogs were treated daily with local application of the antibiotic powder and systemic penicillin and dihydrostreptomycin combination at a rate of 1 ml/5 kg of body weight intramuscularly. This treatment helped to control the exudate for two months after which the purulent discharge recurred in both dogs.

Macroscopic lesions

At necropsy the gross changes in the three dogs, which did not have complications, were no different than those described for the previous three groups. The conduit was surrounded in the subcutis by a thick zone of granulation tissue. New bone formation around the contact surface between the hub of the conduit and both ribs was observed. The lungs were adhered to each other around the silastic tube forming a cul-de-sac and also adhered to the intercostal incision line.

Two of these dogs (#671 and #666) had Dirofilaria immitis in the right ventricle and pulmonary arteries. The
bronchial lymph nodes were enlarged and edematous.

The fistulous tract with the purulent discharge as seen in dogs #666 and #671 drained between the cutaneous trunci muscle and serratus ventralis muscle. The tracts extended 5-10 cm on the ventro-lateral aspect of the lead system site. A purulent discharge was noticed around the conduit-skin junction in dog #664. This dog did not have any fistulous tracts.

**Microscopic lesions**

Dogs which did not show complications grossly had a thick zone of fibrous connective tissue formed around the conduit. In some areas of tissue contact with conduit in the subcutis, there was proliferation of mature collagenous connective tissue, 1-2 mm thick, while in other areas plasma cells, histiocytes and some neutrophils were present (Figures 53 to 56).

In the three dogs in which infection was evident, the areas of tissue contact with conduit had marked proliferation of capillaries and infiltration with neutrophils, eosinophils, histiocytes and plasma cells. The acute inflammatory zone, 1-2 mm thick, was surrounded by a zone of mature collagenous connective tissue. Tracts with similar inflammatory changes were present through the muscle layers and the subcutis.

The changes in the ribs were similar to those in other groups. Periosteal new bone formation was present at the
Figure 53. Upper left dog #667, 365 days. Tissue reaction around the conduit in the subcutis. Note absence of inflammatory cells. Gomori's trichome stain. X 56

A. Collagen fibers

B. Space occupied by the conduit

Figure 54. Upper right dog #664, 365 days. Villous granulation tissue around the conduit in the subcutis. Numerous plasma cells surrounded by mature granulation tissue. X 56

Figure 55. Lower left dog #665, 365 days. Tissue reaction around one of the spokes of conduit. X 56

A. Mature collagen fibers

B. Fibroblasts

C. Space occupied by the conduit

Figure 56. Lower right dog #668, 365 days. Granulation tissue growth into the threads of the conduit at the subcutis. X 56
periphery of the site of contact of the conduit and ribs. The contact surface was covered by a 1-2 mm thick zone of mature granulation tissue in which a few plasma cells were seen. The infected dogs, #666, #671 and #664, had a villous proliferation of capillaries at the concave depression formed around the conduit in which numerous neutrophils, plasma cells, histiocytes and fibrocytes were present (Figures 57 to 59). Islands of endochondral ossification were found in the periosteal region. Some sclerosis of the marrow in the newly formed bone was evident. In some dogs there was a duplication of the cortex. Focal areas of necrotic debris without inflammatory reaction were seen between the spicules.

The cul-de-sac formed by the lungs around the silastic tube had epithelial hypertrophy, hyperplasia and squamous metaplasia at the lumenal surface (Figures 61 and 62). There were some mitotic figures in the metaplastic region, but the basement membrane was intact. The subepithelial layer was composed of plasma cells, histiocytes and fibrocytes (Figure 60). A thick zone of fibrous connective tissue surrounded the chronic inflammatory zone. The pulmonary side of the sac had an atelectatic zone, 2-3 mm in thickness, infiltrated with plasma cells, histiocytes, and neutrophils. The alveoli adjacent to the chronic inflammatory zone were lined by cuboidal cells.
Figure 57. Dog #664, 365 days. Reaction of the seventh rib to the conduit. Antero-lateral view

A. Groove formed around the lips of the conduit

B. New bone formation around the rim of the conduit

Figure 58. Postero-lateral view of Figure 57

A. New bone formation

B. Groove formed around the ligatures tied around the ribs to secure stability
Figure 59. Upper left dog #671, 365 days. Tissue reaction between the conduit and rib. X 56

A. Granulation tissue
B. Periosteum
C. Bone

Figure 60. Upper right dog #664, 365 days. Cul-de-sac formed around the silastic tube by the lungs. X 140

A. Plasma cells and histiocytes
B. Mature collagen fibers

Figure 61. Lower left dog #666, 365 days. Reaction of the lung around the silastic tube. X 56

A. Epithelial hyperplasia and squamous metaplasia on the lumenal surface
B. Granulation tissue

Figure 62. Lower right dog #666, 365 days. Reaction of the lung around the silastic tube. X 56

A. Polymorphonuclear cells and plasma cells in the lumen
B. Epithelial hyperplasia and squamous metaplasia
C. Granulation tissue
The infected dogs, #666, #664 and #671, had a purulent exudate in the lumen of the sac characterized by severe accumulations of neutrophils, and plasma cells. Proliferation of capillaries on the surface of the lumen with severe infiltration with inflammatory cells was evident. In these dogs, squamous metaplasia was not as prominent as in the uninfected dogs.

Dogs #671 and #667 who had Dirofilaria immitis had considerable endothelial proliferation in the pulmonary artery and arterioles. Medial hypertrophy was present in some of the arterioles and multiple focal lymphoid hyperplasia in the lungs. Their bronchial lymph nodes had chronic lymphadenitis.

**Bacteriological examination of Group 4**

A midtrial culture of the conduit-skin junctions in this group of dogs, *Staphylococcus aureus* was isolated from three dogs. One of these dogs, #671, also had *Proteus vulgaris*. *Proteus vulgaris* was isolated from two additional dogs (#665 and #666).

At necropsy *Proteus vulgaris* was isolated from the conduit-skin junctions of the same three dogs which had carried the organisms. The same organism was cultured from the deep intrathoracic portion of the lead system in two dogs, #666 and #671.

No *Staphylococcus aureus* was isolated at necropsy from
the superficial or intrathoracic portion of the lead system. *Streptococcus canis* was cultured from the swabs of the superficial site of conduit-skin junction in dog #665 and from the intrathoracic portion of dog #664 (Table 1).
DISCUSSION

The continuous search for thoracic artificial organs also includes the search for more satisfactory lead systems. The thoracic percutaneous lead system in this investigation was designed to provide stability to multi-purpose lead systems, to evoke minimal tissue reactions and to control or minimize infection. Studying the effect of a pulsating device on the ribs was another aspect of this project.

The intercostal site was chosen because it would provide a short route to the heart and lungs. The ribs could be used to provide stability to the device, and to anchor the lead system. The upper third of the sixth left intercostal space was selected so that the tube of the lead system would rest between the diaphragmatic and cardiac lobes of the lung and contact the base of the heart. Theoretically, placing the tube at this site provides adequate pulsation to study this effect on the ribs.

In a pilot project, a 1 cm portion of the sixth rib was removed and the conduit portion of the lead system was secured between the free ends of the rib with stainless steel wires. This was not successful because of bone lysis and unstable positioning. Therefore, the conduit portion of the lead system was modified to provide extra stability and a lip was placed on the thoracic end of the hub. The lip was designed to fit under the ribs to prevent movement.
of the conduit. The rim and spokes of the conduit also provided stability by allowing tissue to grow between the spokes. The intercostal portion of the implant was designed for a tight fit between the ribs. The pressure was to stimulate some periosteal new bone formation and thick fibrous tissue to add more stability to the device.

The periosteal new bone formation was very extensive and more than expected. Thickening of the ribs in the majority of dogs was two to three times the size of a normal rib and the extensive eccentric periosteal new bone formation around the teflon conduit was an undesirable reaction. In two dogs (#672 and #674) non-union rib fractures were present. One of these dogs (#672) had lysis of the other involved rib with a pseudarthrosis forming.

The cause of these changes in the ribs was difficult to assess. Pulsation of the device, pressure on the ribs, tissue reaction to the teflon and infection were factors to be considered. Pulsating aortic aneurysm in cases of human syphilis causes erosion of the vertebral bodies or sternum, while the intervertebral disc resists any destructive effect (Boyd, 1961). Therefore, if a more pliable material such as silicone rubber is used instead of the rigid teflon, it may result in less traumatism and less periosteal new bone formation of the ribs. Continuous pressure on periosteum causes irritation and results in new periosteal bone formation or exostosis. Friction between the ribs and
the teflon at each respiratory cycle is an additional irritating factor.

Teflon was selected for the intercostal portion of the thoracic percutaneous lead system because it met most of the characteristics of an ideal prosthetic material set by Scales (1953). Its rigid consistency resembled bone. When placed between two ribs, it provided protection for the silicone rubber tube and stability to the lead system. The rigidity of teflon helped to prevent mutilation by the dog.

Silicone rubber was thought to be the most satisfactory material for the tube portion of the lead system. Tissues did not adhere to the silicone rubber, but a thin fibrous tissue encapsulated it. Several forms of medical grade silicone rubbers were available. Tubes of various thicknesses and calibers were utilized. The large silastic tubes used in this study were of sufficient size to accommodate several smaller sized tubes and wire leads. This outer tube provided protection to the inner tubes or wires from tissue reactions and protected the tissues from external contamination. The inner tubes are suggested to be used for power lines for an artificial heart and could contain air lines, liquids or electric wires. A colored indicator fluid is proposed to be placed inside the outer tube to assist in locating tube leaks.

In some dogs, there was evidence of infection in the
intrathoracic tissues surrounding the silastic tubes. It appeared that the infection had originated in the superficial tissues.

In the future, long acting potent chemotherapeutic drugs or antibiotics would be recommended to be incorporated in the silicone rubber to be gradually released and help prevent bacterial infection.

Shorter and thicker tubing in the lead system is desirable, because it causes less tissue reaction, tolerates more pressure and functions longer. To avoid some of the excessive tissue reactions in the ribs, silicone rubber is proposed to substitute for the teflon and act as a cushion to minimize the irritation to the periosteum. To avoid contact with bone, it is suggested to pass the tube through the diaphragm and to modify the conduit portion of the lead system for the abdominal wall. However, in this case, a longer tube is needed which would fatigue faster, cause more tissue reaction, be less stable and predispose the tissues to infection.

The extrusion of the teflon conduit through the skin was due to its rigid consistency, friction with the tissues and the presence of infection. It is known that silicone rubber is well tolerated in the subcutical region as recommended by Marzoni et al. (1959), Beekhuis 1964, Freeman et al. 1965, and 1966. Thus the substitution of silicone
rubber for teflon is believed to be better because the material is better tolerated and causes less complications.

The external portion of the teflon conduit was threaded to accommodate the protecting washer and to allow ingrowth of tissue to minimize the possibility of descending infection. However, it did not seem to help reduce infection and the threads increased the surface contact of the teflon with tissues. This is considered to be an undesirable feature. Hall et al. (1966) reported on an attempt to find synthetic materials suitable for artificial skin but their attempts were not fruitful. In the near future if a suitable non-reactive artificial skin is found, then bonding of the artificial skin to the silicone rubber is possible. This provides stability to the lead system and minimizes the probabilities of infection.

Staphylococcus aureus was responsible for major complications around the entry sites of lead systems in human hemodialysis patients as reported by Barry et al. (1963), Henderson et al. (1963) and Pendras and Smith (1966). Incidence of infection around the lead system was significant in this investigation. Local infection was evident in seven dogs. There was no evidence of systemic reaction during the observation period. The results of bacteriological examination are listed in Table 1. Staphylococcus aureus was isolated from the external and thoracic portion of the
lead system in four dogs which constitutes 16.6 percent. *Proteus vulgaris* infection was evident in two dogs, 8.3 percent. *Streptococcus canis* was associated with *Staphylococcus aureus* and *Proteus vulgaris* in one dog in each of the infections. *Pasteurella multocida* was isolated from the infected sites of one dog.

According to Marples (1969), the human skin has its ecological distribution of parasites, fungi and bacteria. *Staphylococcus aureus* is one of the most potential skin pathogens causing wound infections in humans. Williams (1946) stated that 80-90 percent of people may be nasal carriers of the *Staphylococcus aureus* in a ten-week period. The skin *Staphylococcus aureus* in 31 of 36 cases studied were identical to nasal ones. *Staphylococcus aureus* is an original inhabitant of the nostrils of humans. It is found on the cornified layers of the epidermis, hair follicles and sweat glands. Blouse *et al.* (1964) reported that 63 of 150 healthy dogs were intermittent nasal carriers of *Staphylococcus aureus*.

Dogs have a tendency to bite their skin to relieve itching, by conjecture this would spread the oral and nasal microflora to the skin sites. Infection around the lead system in this investigation is attributed mainly to self-inflicted infection. Vaccination of dogs with vaccines made of common potential skin pathogens is believed to
reduce the incidence of infection during the postoperative period. The importance of daily cleaning and topical application of an antibiotic powder to the skin site of the lead system in the post operative period should be emphasized. A systemic antibiotic at this period for at least one week is believed to be rational.

The pulmonary reaction to the silastic tube was very interesting, it consisted of adhesions of the cardiac and diaphragmatic lobes to each other and the formation of a fibrous cul-de-sac around the silastic tube. Fibroblasts were lining the lumenal surface of the sac at the end of 30 days observation period. The lumenal surface of the sac after 90 days and up to 365 days consisted of epithelial cells undergoing hypertrophy, hyperplasia and metaplasia into squamous epithelium.

The origin of the epithelium was probably from the respiratory bronchioles or bronchioles. The epithelial cells varied from ciliated columnar cells to cuboidal and squamous cells. There were numerous mitotic figures in the hypertrophic and hyperplastic areas of the epithelial surface. The silastic tube may have penetrated through the fibrous tissue into the lung. The continuous friction caused by each respiratory movement stimulated the proliferative changes on the epithelial surfaces. This could also have attributed to the reaction of the pulmonary tissues to
the silastic material. The basement membrane of the squamous epithelium was intact, therefore those proliferative changes were considered metaplastic rather than anaplastic. Any metaplastic change could be a potential future anaplastic change. Although the longest observation period in this study was 365 days, a longer observation period is needed to evaluate the full effect of silicone rubber on the pulmonary tissues.

Fibroblastic activity was evident in most of the tissues contacting teflon or silicone rubber. The cellular patterns of the fibrocytes and fibroblasts were of orderly arrangement and no anaplastic activity was seen in any of the sections. Foreign body giant cells were not observed in the tissue reactions to teflon or silicone in this study.
SUMMARY AND CONCLUSIONS

1. The goal of this project was to develop and evaluate an effective long-term thoracic percutaneous lead system which could be utilized in present and future cardiac research in Biomedical Engineering.

2. In the design and fabrication of the lead system the following major factors were considered: 1) Stability of a pulsating lead, 2) Prevention and/or control of infection in tissues surrounding the lead system, and 3) Adaptability for multipurpose lead systems.

3. Teflon and silicone rubber were selected for fabrication of the lead system because of their favorable prosthetic characteristics.

4. The lead system had two major parts; an intercostal teflon portion which was designated as a conduit, and a silicone rubber tube. The tube passed through, then was bonded to the teflon conduit. A lip was provided on one side of the conduit to fit under the ribs, a circular rim was reinforced with four spokes attached to the hub of the conduit at the subcutaneous region to allow tissue growth and provide stability. The external portion of the hub was threaded to anchor a teflon washer which was used as a protecting shield.

5. The lead system was implanted at the upper third of the left sixth intercostal space of 24 mongrel dogs and
observed for periods of 30, 90, 210, and 365 days. The silicone rubber tube extended 50 mm into the thoracic cavity between the cardiac and diaphragmatic lobe and touched the base of the heart. This positioning provided the pulsating effect needed in this investigation. A local antibiotic powder was applied daily around the conduit-skin junction for two weeks.

6. Minimal tissue reaction was elicited in the skin and subcutis of 17 dogs. This reaction was characterized by proliferation of fibrous connective tissue around the teflon conduit. Plasma cells and occasional histiocytes infiltrated the tissue at the contact surface with teflon. Fistulous tracts draining at the ventral aspect of the thoracic wall were noticed in three dogs. A portion of the rim of the conduit extruded through the skin in four dogs. Infection in the seven complications extended from the skin to the intrathoracic sites of the lead system. The reaction around the infected areas was local chronic inflammatory in type.

7. The reaction of the ribs around the teflon conduit consisted of excessive periosteal new bone formation and extensive thickening of the ribs at the contact sites. There was a fracture in two ribs and lysis in a rib with formation of pseudarthrosis at the contact sites. Tissue reaction around the teflon conduit was extensive
and unfavorable. These changes were attributed to the rigid consistency of the teflon conduit and the pulsating effect of the lead system.

8. The pulmonary reaction around the silicone rubber tubing consisted of adhesions of the cardiac and diaphragmatic lobes to each other and formation of a thick fibrous cul-de-sac around the lead. Plasma cells and histiocytes infiltrated through the fibrous connective tissue. The luminal surface of the sac was covered by a zone of fibroblasts differentiating into fibrocytes in deeper layers toward the pulmonary tissue 30 days after implantation. The more chronic implantations showed a unique tissue reaction on the luminal surface of the cul-de-sacs which were characterized by proliferation of an epithelial layer on the surface undergoing hyper trophy, hyperplasia and squamous metaplasia. The origin of these cells suggested that they were derived from the bronchioles or respiratory bronchioles.

9. There was no anaplasia around the silicone rubber and teflon portions of the lead system. The metaplasia in the pulmonary tissue surrounding the silastic tube could be potential of anaplastic change. Longer observation periods would be needed for further evaluation of the pulmonary reaction to silastic.
10. Local infection occurred in seven dogs. *Staphylococcus aureus* was isolated from four of these (16.6 percent), *Proteus vulgaris* from two dogs (8.3 percent), *Streptococcus canis* was associated with *Staphylococcus aureus* and *Proteus vulgaris* in one dog each. *Pasteurella multocida* was cultured from one dog.

11. Incorporation of a long acting antibiotic or chemotherapeutic agent in the materials of the lead system is possible and is recommended for prevention of infection.

12. Substitution of teflon with silastic in the conduit portion would probably minimize osseous tissue reaction in the ribs and prevent the destructive effect of pulsation.

13. With slight modification this intrathoracic lead system should be better tolerated and adapted for artificial hearts or lungs.

14. A longer observation period is needed for further evaluation of the lead system.
BIBLIOGRAPHY


ACKNOWLEDGMENTS

The author wishes to express his sincere appreciation to the following people for their excellent teaching, training, advice, and encouragement during the last five years:

To Dr. Phillip T. Pearson, for his great interest, help, and the long hours spent in preparation of this manuscript; to Dr. Frank K. Ramsey for his fatherly attitude and constructive criticisms; to Dr. Wallace M. Wass for his great help and assistance in providing the opportunity to gain the experience in Veterinary Clinical Sciences; to Dr. Neal R. Cholvin for his great interest, advice, and provision of the facilities from the Biomedical Engineering Program during this investigation.

The author wishes also to acknowledge the following individuals: Dr. Benton W. Buttrey for serving in the graduate advisory committee; Dr. Dale D. Gillette for his suggestions; Dr. Robert W. Carithers; Mrs. Barbara J. Royer and Dr. Roger Rehmel for their help; to Dr. Roger M. Hogle for his help in the bacteriological examinations; to Mrs. Grace Faber, Mrs. Alvina P. Owenson, Mrs. Susan Devine, and Mrs. Lois Dille for their excellent work and help in preparation of the histological slides; to Mrs. Andrew J. Wunderlich for making the teflon conduit; to Mr. Charles Deutsch for the photographic service; Mrs. Maxine Kelman
for the typing of the thesis.

The help and encouragement of the staff members of the Department of Veterinary Pathology and the Department of Veterinary Clinical Sciences are greatly appreciated.

This project was supported by funds from the Iowa Heart Association. This support was greatly appreciated and without it this project would not have been possible.

A thank-you goes to the Government of the Republic of Iraq for providing the scholarship.

A special thanks to Suhaila, for her patience, help, and understanding.