ELECTRODE IMPLANTATION IN THE HUMAN BODY

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INTRODUCTION

Many types of electrodes are being used today for a wide variety of clinical purposes. Interest has focused on these electrodes, or more specifically, the electrode-tissue interfaces, because they constitute the true junction between the living tissue and the equipment being employed to study it. Whether the electrodes are being used to monitor potentials or to pass currents, their properties influence the interaction between the equipment used and the physiological system being confronted. Both the effectiveness of the attempted procedure and the actual safety of the patient depend upon our understanding the properties of the electrodes being used.

The purpose of this project is to provide a survey of the various factors involved in electrode applications, and to allow a comparison and evaluation of these factors so that it is possible to determine the best methods presently available to accomplish specific clinical objectives. The review itself is selective rather than extensive. This approach was adopted in order to inform the expert in a given field of recent developments in other related fields and also to educate the newcomer to the properties and uses of implanted electrodes.

The material upon which this review is based was obtained from an extensive computer search. The breakdown of sources, years searched, and number of references utilized is as follows:

*This project was supported by the Veterans Administration, Contract Number V101(134)P-204, in cooperation with the Brain Research Institute, University of California, Los Angeles. Reprinted from a 1974 report that was prepared for limited distribution.*
From these sources were selected around 1,000 references most closely related to clinical applications of implanted electrodes. In addition to references dealing with chronically implanted electrodes in humans, some dealing with acute procedures, animal studies, or surface electrodes were included if they appeared relevant.

Finally, from the 1,000 or so most relevant references, around 100 were selected for the core of the review. In some of the major sections (heart, brain, or muscle) these references were supplemented with some older papers so as to provide a better groundwork for the newcomer. Otherwise the review is intended to be a sampling of current activity within each area.

PHYSICAL AND CHEMICAL FACTORS AFFECTING IMPLANTED ELECTRODES

Almost every investigator who has used implanted electrodes for either recording or stimulating has encountered problems involving the
electrodes. If one feature of implanted electrodes has to be singled out as the underlying cause of these difficulties, then it is the interface existing between the metal of the electrode and the biological medium surrounding it.

This interface exerts its influence on electrode behavior because, whether the electrode is used for recording or stimulating, current must flow through the interface. In the biological medium, this current is carried by charged ions, while in the metal of the electrode it is carried by electrons. In order for a continuous current to flow, there must be some type of mechanism to transfer charge between these two carriers. This charge transfer at the metal-electrolyte interface is subject to a number of physical variations and is one of the main sources of impedance seen in electrode-tissue systems.

The physical structure of the metal-tissue interface influences its behavior (Bikerman, 1958; Butler, 1951; Conway, 1965; Delahay and Tobias, 1961; Glasstone, 1946). If a piece of metal is placed in an electrolyte, physical forces attempt to establish a thermodynamic equilibrium between the two mediums. This results in the establishment of a voltage across the interface, which in turn causes an attraction and ordering of ions from the electrolyte. The ions become arranged in a layer which becomes progressively more random the farther away from the metal surface it is encountered. This layer of charged ions facing the metal surface is called the “double layer” and physically accounts for some of the electrode capacitance.

Besides this ordering of ions around the electrode, the detailed structure of the metal surface must also be considered in accounting for electrode behavior. For any real metal implanted in the body, the metal surface is not homogeneous, but is composed of a mosaic of microcrystalline regions with different physical and chemical properties. Regions of this surface are also covered by adsorbed organic materials, or are insulated under oxides or films of other organic or inorganic materials. These films can all be in a state of flux and can alternately expose and cover regions of the metal surface, resulting in constant changes as freshly exposed regions attempt to reach equilibrium with the electrolyte and with adjacent regions on the metal surface. The different physical properties of these adjacent microregions result in local miniature battery effects with current flowing between them.

Dynamic chemical reactions underlie the potential across the metal electrolyte interface. The most commonly cited reaction is one in which an atom from the metal becomes a hydrated ion in the electrolyte, with its electrons remaining behind in the metal. In practice, many more reactions are possible, such as gas evolution and other inorganic reactions, organic reactions, and reactions of the redox type involving only charge exchange with the electrode.
All of these reactions are capable of occurring simultaneously at the metal surface with the potential across the interface being determined by whichever chemical reaction is in control at the moment. If an external current is passed through the electrode, the reactions which are able to supply the most current become predominant. When sufficient current is forced through the interface, the potential can rise sufficiently to enable new types of reaction mechanisms to take place to carry the current.

This complex interface is the location through which current must flow in any application utilizing electrodes. In the case of recording, the currents passing through the interface are usually very small. Unlike electrical stimulation, they generally do not polarize the electrode (although any electrode undergoes some polarization when current is passed through it).

Electrical equivalent-circuit circuits are sometimes proposed to account for the behavior of the interface. As long as one bears in mind the underlying chemistry of the interface, these electrical models can be quite useful in dealing with the practical engineering aspects of electrodes. One of the simplest equivalent circuits consists of a resistor and capacitor connected in a parallel connection. At a fixed frequency and voltage, this circuit describes the electrical behavior of the interfacial impedance, and points out that for any waveform being passed through the interface, part of the signal is passed as a capacitive current. This is important since capacitive currents do not place demands on the electrode as do faradic currents.

For any given frequency, values for the resistor and capacitor in the equivalent circuit can be calculated. However, these values are found to be frequency-dependent, with both the resistance and the reactance of the electrode decreasing as the frequency is increased. The resistance and capacitance are also influenced by the voltage across the interface, with the resistance dropping and the capacitance becoming larger at higher voltages. These features are illustrated for experimental data in Figures 1 and 2.

A list of problems encountered when recording with implanted electrodes could include d.c. offset, electromagnetic and electrostatic interference, cable and electrode movement artifacts, tissue toxicity, noise, impedance matching, and spontaneous polarography (Dymond, 1974; Gatzke, 1974; Geddes, 1972; Huhta and Webster, 1974). Some of these items are only indirectly due to the electrode properties, while others are directly electrode-related.

\[\text{For present purposes, polarization can be defined as a change from the mean value of the potential across the interface when zero net current is flowing.}\]
The d.c. offset of electrodes is a basic characteristic of the interface and large or changing offsets can have significant consequences when recording. The potential seen in any real system is actually the sum of two electrode potentials (called half-cell potentials), since two electrodes are needed to record a voltage difference from the body.

The d.c. potential resulting from one electrode is due to chemical reactions at the surface. Electrodes made of different materials are well known to have different potentials. However, electrodes of the same material may have different potentials and, in fact, it is difficult to make them so they do not.

Why this is so can be understood by taking a closer look at the equation for the half-cell potential of a metal electrode whose potential is determined by the mechanism of release of metal ions into the solution (Conway, 1965). The net chemical reaction is
\[ M_{(metal)} = M_{(soln)}^{Z^+} + ze^-_{(metal)} \]

and the voltage across the interface is given by

\[ V = V_O + \frac{RT}{F} \ln a_{(M^{Z^+})} \]

where \( V_O \) is the voltage when the ionic activity equals unity. \( V_O \) is abulated as a constant for different materials, but it is a constant only under closely controlled experimental conditions and can itself be broken down into a number of other constants. These constants can be deduced if the controlling chemical reaction is expanded to include the intermediate steps. For the above metal dissolution reaction, these steps are sublimation of the metal, ionization of the free metal atoms, solvation of the metal ions back into the electrolyte, and solvation of the free electrons back into the metal. The term “\( V_O \)” then has hidden within it energies of sublimation, ionization, ion solvation, and electronic work function (for returning the free electrons to the metal). Some of these terms are dependent upon the microcrystalline condition of the metal surface, and any physical changes in the electrode will modify the half-cell potential. These considerations apply in general to other types of voltage-controlling reactions at the metal surface and result in difficulty in making two electrodes which have the same voltage.

Spontaneous polarography (Clark and Sachs, 1968) can occur because of these different electrode voltages, if proper precautions are not taken. It occurs when two electrodes with different half-cell potentials are connected directly together or through a low impedance. The electrodes then can act as a battery, and a current will flow through the completed circuit. This could have serious consequences for both the electrodes and the surrounding tissues.

Noise and artifacts present another source of problems when recording. Movement of the wires leading to electrodes can cause artifacts due to currents induced in the wires. Movement of the electrode itself can produce artifacts caused by mechanical disturbance of the layer of charge surrounding the electrode and through interference with the chemical equilibrium conditions existing at the electrode.

In the absence of movement, artifacts can arise due to the spontaneously occurring microchanges in the equilibrium conditions at the electrode surface, as well as to changes in the concentrations of species in the environment surrounding the electrode.

Electrode impedance properties must be frequently considered when recording with implanted electrodes. The electrical impedance of the interface is high at low frequencies and decreases as the frequency of
the test signal is raised. This frequency-dependent source impedance places requirements on the amplifiers used to make the recording. The general rule is for the input impedance of the recording amplifiers to be much larger than the impedance of the source of the recording. This source impedance is composed of the impedance of the tissue and the impedance of the electrodes, or more specifically, of the electrode-tissue interface. In low frequency considerations (less than a few hundred Hz), the majority of the source impedance is usually contributed by the interface. Since the impedance of electrodes is largest at low frequencies, it is in this region that the greatest problems arise. Also, since electrode impedance is inversely related to the size of the active exposed surface area, this problem of impedance is greater for small electrodes.

If this source impedance becomes comparable to the amplifier input impedance, the signal recorded can be significantly attenuated. This results in a distortion of the low-frequency components of the recorded waveform as has been demonstrated for the EKG by Geddes and Baker (1966).

**Figure 2.**—Dependence of the series-equivalent reactance $X$ on frequency and current density; stainless steel electrode (0.157 cm$^2$) in contact with 0.9 percent saline. (From Geddes et al., 1971.)
When implanted metal electrodes are used for stimulation, the problems are greatly compounded. The electrode interface is significantly disturbed from its equilibrium position by the currents being passed through it. This can cause large changes in the electrical impedance which can interfere with the operation of stimulation equipment. Undesirable chemical reactions can occur, such as metal erosion, and tissue can be subjected to thermal or chemical damage. The consequences of his stimulation can be approached by considering the interaction of the stimulus pulse shape and amplitude, since combined they affect net chemical reactions occurring at the interface. Many of the difficulties with stimulation electrodes arise through the faradic charge transfer mechanisms occurring during stimulation and can be minimized when the faradic portion of the current is reduced or neutralized.

The frequency composition of a waveform of short duration is higher than for a long one. This in turn increases the proportion of the signal which can be passed through the interface as capacitive current, rather than by faradic mechanisms. This simple fact in part underlies the result demonstrated in numerous studies that short pulses produce less electrode and tissue damage. As a consequence, a general policy when stimulating is to limit the duration of the waveform used.

Both the duration and amplitude of a pulse can be seen to directly influence the chemical reactions at an electrode. As current from an applied pulse first begins to pass through the interface, much of the current will be carried in part by charging in the double layer. Naturally, this layer can only accommodate so much charging, and this level will be reached faster if the pulse amplitude is high. Past this point, the current must be increasingly transferred through chemical reactions. The exact nature of these reactions can be very complex and is determined by the characteristics of the stimulus waveform, the electrode material, and the compounds available from the tissue. As a stimulus continues, one type of reaction can be replaced by another as the interface is driven further and further from equilibrium.

In discussing electrodes used for stimulation, Brummer and Turner (1972) have pointed to four different types of chemical reactions: electrolysis of water, oxidation of saline, oxidation of the metal, and oxidation of organics.

Electrolysis of water is damaging since it produces gases. Oxidation of saline can produce many different compounds, some of which, such as $\cdot OH$, are toxic.

Oxidation of metal releases metal ions and salts into the tissues and is invariably dangerous. Although some metals are known to be less prone to erode than others (i.e., platinum will withstand stimulus currents better than stainless steel), all bare metals are eroded under sufficiently
rigorous conditions and the resulting ions and salts are to some degree toxic.

Finally, oxidation of organics in a true situation with an electrode directly stimulating tissue is a complex problem whose consequences are not clearly known. Basically, the question centers on the quantities and toxicities of the chemical products formed.

These mechanisms can be damaging to both the electrode and to the surrounding tissue but can be reduced if the need to transfer charge by faradic mechanisms is lessened. This can clearly be done by reducing the pulse durations and amplitudes. An alternate reduction of the problem can be achieved if the chemical changes at the electrode could be rapidly reversed before any damage was done. This solution underlies the use of biphasic stimulation waveforms, such as have been advocated by Lilly (1961). These biphasic waveforms, illustrated in Figure 3, have been shown to be much more effective in preventing electrode and tissue damage than monophasic waveforms. Presumably, this effect is brought about by the second half of the waveform canceling the deleterious chemical effects caused by the first part.

The proper application of this biphasic technique must lead to a more careful consideration of constant current versus constant voltage stimu-

![Figure 3. Waveform of stimulating current: pulse pairs of current resulting from quasi-differentiation, with passive electrical elements, of a rectangular pulse. Measured: 2 percent of the peak, the duration of the positive pulse (upward) is 34 µsec., and the duration of the negative pulse (downward) is 28 µsec. The areas under the two pulses are equal; therefore the negative coulomb flow is zero for the pulse pair algebraically summed during a time interval of 200 µsec. from the beginning of the positive pulse. (From Lilly et al., 1955.)](image-url)
For constant voltage stimulation, there is an initial large current flow, in part due to initial double layer charging, which then declines to a lower constant level. When the voltage is removed, the electrode interface discharges. For constant current stimulation the voltage rises, and if the pulse were to continue long enough, the voltage would stabilize at a level characterized by the chemical reaction capable of supplying the steady-state current and by concentration gradients in the medium surrounding the electrode.

For constant voltage stimulation, the current waveform is not identical to the voltage waveform, is not identical for positive and negative pulses,
and makes it difficult to match and cancel the chemical reactions caused by the first pulse. This is not the case for constant current stimulation, and although the resulting voltages for currents of opposite polarity are not matched, the chemical reactions are symmetrical. This is one reason why constant current stimulation is recommended.

In practice, it may be more appropriate to specify the amount of charge being passed per half pulse when reporting stimulation parameters. This charge is related to the product of current and pulse duration and tends to describe their combined effect. Maximum safe stimulation levels should probably be stated in charge per unit of active surface area of the electrode.

The problems when recording or stimulating with implanted metal electrodes are inherently associated with the passage of current through the metal-tissue interface. Although many steps can be taken to minimize these difficulties, the problem is fundamental and remains. One attempt to get around it is to insulate the active metal surface with some type of dielectric material. This procedure has been used for both recording and stimulating electrodes. Although it presents problems in its own right, such as high electrode source impedances, there are obvious advantages in having the bare metal surface covered. The use of dielectric materials such as tantalum pentoxide restricts all of the current flowing through the interface to a capacitive nature. The dielectric material is chosen to have as high a capacitance as possible. The amount of current flowing in stimulation is inherently limited to the amount which can be passed by charging the interface. Although this technique is still developmental, it offers much potential for use in chronic stimulation devices such as visual or auditory prostheses (Guyton and Hambrecht, 1974).

Coupled with this search for new materials for the electrode interface, parallel work using new materials and fabrication techniques to construct entire electrodes is under way. Work also continues on other methods of delivering stimulation to the tissues, such as with beamed ultrasonic or electromagnetic energy.

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*An additional reason involves the effect of stimulation on the tissues. The force exerted on ions in the tissues is proportional to the current flowing between the electrodes and not to the applied voltage which has a waveform different from that of the current and exists in large part across the interface, rather than across the tissue. Hence, controlling the stimulus actually applied to the tissues implies controlling the current passed.*
STIMULATING ELECTRODES

Brain Stimulation

The underlying assumption in implanting a stimulating electrode in the human brain is that passage of current through the electrode will produce an effect which closely resembles the effect of the activity, be it normal or abnormal, which usually occurs at that site. Achieving this is not simply a matter of using sufficient stimulus intensity to excite brain tissue. The task is far more complex because brain tissue is not homogeneous and a single implanted electrode may be adjacent to both excitatory and inhibitory centers as well as centers controlling a variety of behavioral or bodily functions, each with their respective thresholds of excitation. Furthermore, the same electrode could be near a neural conducting pathway so that the effects of stimulation may reflect the functioning of neural tissue quite remote from the site of stimulation. Finally, the parameters of stimulation, regardless of what they are, can in no way be considered to imitate normal activity at that site, nor will the activity be occurring in its normal functional context.

In fact, normal activity is not even strictly electrical, but rather is electrochemical in nature, and it has even been suggested that alternate techniques of stimulation may be required to imitate normal functioning. The major advantage of using electrical stimulation as opposed to ionic, humoral, or other electrochemical techniques lies in the fact that the experimenter has comparatively good control at least over the independent variables. Electrodes and implantation techniques have been standardized so that sites of stimulation can be confirmed by X-ray and histology, and stimulus parameters (pulse length, shape, intensity, and frequency) can be controlled and measured. On the other hand, even though electrochemical events themselves may be well understood, the rates and extents of chemical diffusion make it difficult to delimit stimulation effects.

A further complication of brain stimulation studies lies in the difficulty which sometimes is involved in assessing the effectiveness of stimulation, as Mickle (1961) among others has pointed out. When stimulation is in classical motor or sensory systems, overt movements can be quantified and sensory reports can be standardized. Autonomic responses are likewise accessible to measurement. What presents a problem, however, is the fact that identical stimulation parameters may produce either variable effects on the organism or no measurable behavioral or subjective responses whatsoever. Arguments can be made, in such cases, for assessing the effects of stimulation by direct recording from within the nervous system itself, somewhere near the site of stimulation. This presents a host of new problems; in addition, what one finds will depend on where one looks.
Despite these limiting factors, stimulating electrodes have been implanted in the human brain in a large number of different areas. For ethical reasons use of stimulating electrodes has been justified for only two major purposes: as an aid to the diagnosis of brain pathology (prior to ablation or lesioning), and as a prosthetic device.

As a representative example of the first purpose, stimulation may aid in delimiting the pathological area, such as in temporal lobe epilepsy (Crandall et al., 1963). When epileptic tissue is stimulated, slow rhythmic after-discharges are found more often than in normal tissue. Furthermore, stimulation in pathological tissue often reproduces features of the spontaneous clinical seizure. This technique has been especially useful in candidates for surgery where it is difficult to establish the existence of or to localize the focus of a seizure by other clinical diagnostic techniques. In instances where therapeutic lesions are to be placed in standard pathways to alleviate the symptoms of such maladies as chorea, Parkinson’s tremor, or thalamic pain syndrome (Nashold and Wilson, 1970), stimulating electrodes are used to locate and determine the site of future lesioning.

Work is already well under way to design systems for chronic stimulation of primary sensory cortex which will act as visual (Brindley and Lewin, 1968) and auditory (Dobelle et al., 1973) prostheses.

**Diagnostic Electrodes**

A prerequisite to any study of the human brain employing stimulating electrodes requires accurate placement in the target site, since structures are small and a deviation of only a few millimeters can result in change or failure of the effect. Stereotaxic placement in animals is a relatively simple matter since atlases are available and one need only obtain an animal of appropriate size and species. In humans, the task is more complex partly because the relation of brain structure to bony landmarks is so variable and partly because an error of placement is so much more crucial than it would be in an animal. As in animals, the human system is based on a three-dimensional coordinate system. The main difference lies in the fact that instead of using bony reference points (inferior orbital arches and the auditory canals) as in animals, intracerebral landmarks are used such as the pineal body or the ventricles, the foramen of Munro, and the anterior and posterior commissures, visualized by means of opaque dyes or air and X-rays.

Details of stereotaxic surgery are not within the scope of this review. Nevertheless, a few critical factors are worth mentioning. References in Spiegel and Wycis (1961) contain additional information. The median plane through the brain must lie parallel to the X-ray film and must be a constant distance from it and from the X-ray tube in order that the measurements (done on the developed film) will have meaning (Spiegel...
Furthermore, these distances can affect electrode visibility (Dymond et al., 1972). Electrodes must be radio-opaque to show up on the film, X-rays should be taken to confirm placement, and, where possible, there should be histological followups. Despite great care regarding placement accuracy, electrodes are often found to be 1 to 2 mm. off target (Spiegel and Wycis, 1961) and it may therefore be wise to use multiple rather than single contact electrodes.

A word can also be said about the actual electrode insertion. The angle of insertion should be such as to avoid hitting any structures which might damage or deflect the electrode. When insertion guides are employed, care must also be taken that insertion is not impeded as the electrode advances.

The body will react to the implanted electrode, partly because it is a foreign body and partly because current is being passed through the tip, resulting in the dispersal of electrolytic byproducts into surrounding tissue. In choosing electrode materials it is wise to consider the body's reaction both to the passive implant and to one to which current is applied. In addition, the length of time the material is to be implanted may have bearing on the type of material chosen.

Implantation of the electrode first causes local neural and vascular damage which in turn produces edema and white blood cell migration. Restorative processes then take place—damaged tissue is absorbed, blood vessels multiply, and the electrode becomes encapsulated in a thin layer of fibrous tissue. Providing that electrode materials are nontoxic, the remaining tissue is normal and the capsule will not interfere with conduction. Two to 4 weeks after implantation, the tissue should have stabilized (Delgado, 1969).

Tissue reaction to the implanted electrode can be minimized by proper selection of both electrode and insulation materials. Implanting in brain tissue for 2 months without passage of current showed platinum, platinum-8 percent tungsten, platinum-10 percent rhodium, platinum-10 percent iridium, platinum-10 percent nickel, platinized platinum, a gold-nickel-chromium alloy, a gold-palladium-rhodium alloy, a chromium-nickel-molybdenum alloy (Vitallium), stainless steel, rhenium, gold and boron to be nontoxic (Dymond et al., 1970). Silver (Dymond et al., 1970), silver chloride, and copper (Fischer et al., 1961) are highly toxic.

Passage of current, however, can cause changes in the electrode or surrounding tissue (due to release of metal ions) which can render them inadvisable materials. Tungsten, stainless steel, and silver tend to mushroom at the tip (Loucks et al., 1959); and furthermore, passage of current through stainless steel deposits iron, which has been demonstrated to excite tissue in the hypothalamus by its presence (Ervin and
Kenney, 1971). Platinum-iridium is less prone and is often used as an electrode material.

Most insulating materials currently in use seem to be nontoxic. Insl-X Epoxylite, Teflon (Ervin and Kenney, 1971), Tygon, Formvar, Thermobond M-472, and Polyethylene (Fischer et al., 1961) all seem to be well tolerated. The choice must depend on other factors such as ease of manufacture, mechanical properties (beading, flexibility), and the ability to withstand current passage. With respect to the latter point, vinyl-based insulating materials (such as Insl-X) tend to pull away from the electrode. Teflon, too, may develop microcracks unless specially bonded to the metal (Ervin and Kenney, 1971).

In choosing materials to use, some thought must also be given to the length of time the implant is to remain in the brain. For most diagnostic purposes, electrodes need not be left in place for more than a few weeks or a few months at the most. From war and injury cases there is already much evidence that plastics, wires, and plates can remain in the body, as passive implants, for virtually lifetimes with only mild local reaction: One of the major limiting factors in implanted electrodes is that the path of the connector through the skin provides a potential route for infection. Electrodes have remained in place in humans for extended periods of a year or more (Delgado, 1969).

Nevertheless, stimulating electrodes are not passive and the long range effects of current passage must be considered, as was ably demonstrated in a study by Goddard (1969). He found that repeated stimulation of certain areas of the brain at levels which produced no behavior change, no after-discharge, and no appreciable tissue damage were capable of eventually producing bilateral clonic convulsions. He termed this effect “kindling.” This stimulation, although it had to have minimum intensity, was not related to current parameters, but rather depended on intermittency with an optimal interval of 24 hours or greater. The areas most affected by this stimulation were those related to the limbic system, with the amygdala being the most sensitive. Goddard argued that if a critical mass of tissue is saturated with current, a phenomenon similar to learning takes place, i.e., the brain “learns” to have seizures. How much tissue is stimulated may be the critical factor in these experiments since the phenomenon was very difficult to establish in monkeys requiring a much greater area of stimulation (3 mm.) than is normally stimulated in humans. Nevertheless, caution should be exercised especially when stimulation is done in the limbic structures.

Stevens et al. (1969), stimulating in the lateral amygdala and dorsal hippocampus, found behavioral changes which outlasted the stimulation by minutes or hours. Although they attributed their findings to neurohumoral events, one cannot rule out the possibility that change
similar to those that occur in kindling may be taking place.

It is obvious that the size and shape of an electrode will contribute to the amount of tissue damage done by electrode insertion. The larger the electrode or the more irregular its surface, the greater the trauma induced. It has also been pointed out (Dymond et al., 1972) that the flexibility of an electrode can also contribute to its ability to do damage. That is, an electrode which is too flexible and bends upon insertion or is too rigid and does not “give” with slight movements of the brain is undesirable.

Electrodes come in a wide variety of arrangements but most do not exceed 1 to 2 mm. in diameter. A simple, unsupported monopolar electrode must be fairly rigid (tungsten is a good material) and can be electrolytically etched to a point to facilitate insertion. Finer wires can be mounted on a rigid strut to form bipolar or multipolar electrodes. To avoid gouging of the brain, the tips can be staggered and bridged by insulation (e.g., Crandall et al., 1963) to result in a knife-like effect for smooth entry. More recent studies favor the use of a bundle of fine wires twisted around each other and/or cemented together. The total bundle strength alone may then be great enough for insertion, or the wires may be inserted through hypodermic tubing. Insulation will of course fatten the electrode, the amount depending on the type of material used, its viscosity, and the number of coats applied. Beading of the insulating material can increase the trauma of electrode insertion and must be scrupulously avoided. There is no question that these electrode assemblies are large enough to damage the brain. Nevertheless, their repeated successful usage in diagnostic studies, coupled with the functional redundancy in the nervous system, argues for their continued use.

There are some (e.g., Dymond et al., 1972; Delgado, 1969) who feel there must be enough flexibility in an implanted electrode to allow it to stay in place relative to a given neural structure even as the brain moves about in the cranium because of postural adjustments, blood or cerebrospinal fluid pressure changes, or blows to the head. To accomplish this, Delgado (1969) uses fine flexible wires, which are inserted through stainless steel tubing which is later withdrawn. He also puts a loop of electrode wire where the electrode passes through the skull.

Dymond et al., (1972) thoroughly reviewed factors which must be considered regarding electrode flexibility, not only insofar as brain movement is concerned but also in terms of electrode distortion during handling and insertion. They consider the requirements of stiffness (the resistance to deflection by transverse forces and buckling by axial compressive forces) and strength (the resistance to the tendency to bend permanently with exerted force, or the tendency to break suddenly). The size, shape and unsupported length and surface condition all contribute to these factors. With the criterion of 2 mm. maximum displace-
ment over a 6-cm. insertion route, they conclude that the best materials to use for electrodes are tungsten, rhenium and high-iridium alloys of platinum.

Probably one of the most difficult decisions to make in human stimulation studies is what stimulus parameters to use. No stimulus accurately reflects normal biological activity and many stimuli can damage tissue. Furthermore, different brain structures and purposes dictate different optimal values. At present one can only state what not to do and what range of stimulus parameters seems safe and effective. What not to do is covered in the section of this review dealing with lesioning. The factors which are important in safe stimulation are considered below. Although electrode arrangements can be monopolar, bipolar, or multipolar, the choice lies between monopolar and bipolar stimulation because in multipolar arrangements stimulation usually takes place between only two points at any given time.

In a monopolar arrangement, current, although concentrated at the tip, radiates over a wide area rendering it inappropriate for precise work. This technique would be inadvisable, for instance, where an inhibitory function may be within a few mm. of the target site area.

In bipolar stimulation, current is concentrated between the two tips, lying usually ½ mm. to 2 mm. apart. Where strict anatomical localization is required, this technique is more appropriate. Variations of the bipolar technique include a concentric arrangement with a single wire fixed in the lumen of hypodermic tubing and a multipolar arrangement where a bundle of wires is cemented together. The electrical field is more tightly concentrated in the concentric electrode, and the area being stimulated lies in front of the tip of the electrode, enabling stimulation of a structure not necessarily entered by the electrode (Ervin and Kenney, 1971). In the multipolar case, the experimenter has the advantage of a movable electrode without the attendant trauma, i.e., a number of different sites of stimulation can be chosen but the brain is penetrated only once.

The electrochemical events which occur at the electrode-tissue interface when current is passed are highly complex, involving release of metallic ions into surrounding fluid, corrosion of the electrode, and release of impurities in the metal, as well as changes in the tissue and surrounding fluid. These events are dependent on the geometry of the electrodes, their composition, and the composition of the surrounding fluid and tissue. Not only are they dependent on the current flow, but they in turn can alter the current flow and hence alter the effect of stimulation on neighboring tissue. It is not unusual to find fluctuations in current flow despite seemingly constant input to the electrode.

Except for evoked potentials or reflexes where single, brief pulses are used, the usual form of brain stimulation is a train of electrical pulses. The parameters within a train which can be meaningfully varied are: the
intertrain interval, the length of the train of pulses, the frequency of pulses, and the duty cycle (that portion of the interpulse interval in which current is turned on). As well, each pulse can vary in voltage and waveform. Some of the factors found relevant in “safe” stimulation are considered briefly here. A more detailed presentation, though with different orientation, can be found in the section dealing with lesioning.

As was mentioned earlier, current passage can physically change the electrode itself, which, in turn can cause mechanical trauma and further alter current flow. Loucks et al., (1959) showed erosion as mushrooming of electrode tips in tungsten and stainless steel even with very small currents. Delgado (1964) suggested that erosion can be lessened by using short pulse durations (0.2 msec.).

The major problem in passing current is to prevent electrolytic damage (related to the total coulombs, i.e., the amount of change, passed in one direction through tissue) or thermal damage (related to the total energy, expressed in watts, that passes through tissue; Lilly, 1961). The number of coulombs passed will depend on the magnitude of the applied current, the degree of electrode polarization, the size of the electrode, and the duration of stimulation. In order to study the effects of some of these variables on tissue damage Lilly (1961) used a standard train of unidirectional rectangular pulses (60/sec.), each train lasting 5 sec. and being repeated every 30 sec. Extrapolating from Lilly’s figures, Ervin and Kenney (1971) pointed out that pulse durations of greater than 5 msec. resulted in electrolytic damage; durations of less than 0.2 msec. resulted in thermal damage. A safe range of durations appeared to lie between 0.1 and 1.0 msec., as long as the current was less than 10 ma.

The damage caused by steady or even pulsed d.c. currents can be overcome by using bidirectional pulses. That is, polarity is reversed in midpulse so that the net current flow is equal to zero. Any transient polarization which might still occur can be reduced by using shorter pulses. If pulses are too short, however, higher voltages are needed. Mickle (1961) reported much less tissue damage and polarization effects during prolonged periods of stimulation when pulses where of alternating polarity and equal current (1 msec. pulses; 100/sec.). Some have argued that the waveform of these bidirectional pulses should be sinusoidal. Olds and Milner (1954) used a 60-Hz sine wave current while Lilly et al. (1955) argued that a waveform as illustrated in Figure 3 is preferable.

The main consideration in stimulation studies is the safety of the patient. During stimulation he must be protected from stray d.c. currents but more important from ground to avoid the possibility of lesioning or electrocution. It is therefore common to isolate the patient from the equipment which programs the stimulus. This can be done by use of
a transformer, so that the stimulator drives the primary coil, with the secondary coil being connected to the stimulating electrodes in the patient. One disadvantage of using a transformer is that breaks can occur in insulation which can cause shorts to occur between the primary and secondary windings. This results in direct coupling of the patient with the stimulator, i.e., he is no longer isolated from the high voltages. There are techniques available to prevent this in which the power sources and triggering and timing circuits are not in physical proximity, for example, induction by radio frequency modulation or induction by photon coupling. Such devices are commercially available (e.g., Grass Instruments).

**Prosthetic Devices**

Early work on electrostimulation of the brain during cranial surgery has shown a variety of elementary sensations and movements. In recent years there has been an interest in the feasibility of brain stimulation as a prosthetic technique for blindness, deafness, and possibly paralysis. Although technically difficult, such stimulation is advantageous over more peripheral forms of stimulation because it would be applicable to most sensory deficiencies regardless of what part of the system has failed. Although work is still in the preliminary phase, it does look promising.

There are certain clinical requirements in the area of visual and auditory prostheses. One such requirement is that the device be completely implanted so that there is no pathway through the skin, thus eliminating a potential route for infection. This imposes certain engineering problems.

One major problem is the accessibility of the primary sensory cortex to be stimulated. The primary visual cortex lies along the walls of the calcarine fissure, on the medial surface of the occipital lobes pressing against the falx cerebri. The auditory cortex lies on the superior surface of the temporal lobe within the sylvian fissure and is further protected by the branchings of the middle cerebral artery. Nevertheless Brindley and Lewin (1968) have implanted devices for visual prosthesis in blind subjects and Dobelle and colleagues (1973) have implanted a prototype device in experimental subjects which remained in place for several days. The former device conforms to the exterior surface of the cortex without invading the calcarine fissure; the latter is placed on the lower lip of the sylvian fissure (probably association cortex), which is more accessible than Heschl's gyrus.

Before implanting such a device, tests must be made to determine whether the cortex functions normally. After years of blindness/deafness there may be some deterioration. Certainly there is
evidence (Wiesel and Hubel, 1965) that disuse of the eyes from birth can result in abnormal visual cortex development. This does not, however, preclude stimulation prostheses.

The major stumbling block to implanted cerebral prostheses at present seems to be the unknown effect of prolonged implantation and stimulation on the tissue. Tissue reaction to implanted materials has been covered earlier, but an extensive analysis of these effects has been done by Dobelle et al. (1973). A variety of materials were passively implanted in rabbits and it was found that most were well tolerated unless either there was trauma produced at the time of surgery or the electrode was free to move after implantation. All surface implants were encapsulated by leptomeningeal cells, but with greater trauma there was more evidence of damaged tissue and activity characteristic of body repair. With depth implants trauma tended to produce a “boundary cell” which separated the material from the neural tissue.

Certain stimulus parameters were considered dangerous, producing both damage to underlying cortex and changes in the blood-brain barrier (which according to Mortimer et al. (1970) is an index of damage due to electrical stimulation). Monophasic pulses were the most dangerous for two reasons: toxic electrolytic byproducts can severely alter local pH, and electrophoresis can damage cells.

The implanted array must be miniature and must be capable of performing throughout the waking day with little variation in stimulus parameters. The array must contain enough points to convey meaningful appreciation of the environment (i.e., for vision an interpretable image must be seen, while in hearing speech perception is a major goal). Information should be rapidly transmitted since to justify the surgery risk and expense, the device must be competitive with braille and sign language.

The carrier for the electrodes must be flexible enough to conform and adhere to the cortical (or pial) surface without damaging the brain and must be of effective insulating material so the electrode points are isolated from each other. Each electrode point must be made of nontoxic material, must be of nonirritating configuration and must not corrode during passage of the current. Since thresholds underlying each stimulating point may vary, the stimulus package must be capable of delivering a different stimulus to each electrode. Furthermore, there must be redundancy in circuitry as a “fail-safe” device.

Modern-day technology with printed circuits, transistors, etc., seems capable of handling these requirements. All that is needed is a practical working model and more knowledge of tissue reaction. Marg and colleagues (1970b) have proposed a design for a visual prosthesis which, although as yet untested in humans, proposes a system to satisfy many of these conditions.
The design of Marg et al. (1970b) for a visual prosthesis is as follows: 512 platinum electrodes (9 bits) are woven into a Dacron mesh which is then impregnated with silastic rubber which will conform to the cortical surface. Each electrode is exposed 1 mm\(^2\) to minimize impedance (3,000 ohms resistance) and the electrodes are spaced 1 mm. apart for maximum phosphene resolution. The return path is a strip of platinum foil implanted in the scalp where the ample vascular surface can dispose of electrolytic byproducts.

Circuitry consists of an internal and an external package. The internal package is completely implanted in a hole in the cranium over one hemisphere (see Fig. 5) with a short cable running to the electrode array. The external package is a power unit with rechargeable batteries which is electromagnetically coupled through the skull. Stimulus parameters are biphasic wave pulses with a 20 to 30 v. maximum, 100 to 1,000 usec. duration pulses, and a 100/sec. pulse rate. Details of the circuitry can be obtained from the paper.

The main problem which remains is the translation of the image which falls on the light-sensitive external matrix to the points on the internal electrode array. The implanted array does not extend into the calcarine fissure (primary visual cortex) but remains flat on the medial cortical surface. It is therefore necessary to map the stimulated cortex and arrange an appropriate program so that the external events can be translated into a meaningful stimulus pattern on the cortex surface (and preferably a meaningful phosphene image). Not only does spatial correspondence have to be programmed but appropriate threshold adjustments have to be made at each stimulus point on the cortex surface.

Dobelle et al. (1973) developed an electrode array consisting of 5 mm. platinum wire specially coated with Teflon insulation (their paper contains details and rationale), with the entire unit in the form of a ribbon cable. The array could easily be inserted in a Penrose drain at the time of surgery (for tumor, epilepsy, etc.) and removed several days later without additional surgery. To form an electrode tip, a ball was flame-formed on the end of the wire (avoiding earlier problems of welding on a tip). The ball was then forged to the proper shape and affixed to the Teflon with microscopic locking pins. Their arrangement is shown in Figure 6.

These authors also felt that sufficient technology already exists to render this prosthesis feasible, but that care should be taken regarding the following facts: 1. Manufacturing processes for miniature circuits involve toxic elements which must be cleaned from the surface before use in implantation. 2. Surface flaws on the electrode carrier material can produce reactions because of invasion of tissue. 3. The biological environment may corrode implanted materials. 4. Materials have to withstand the rough handling of implant surgery. 5. Gases used in
FIGURE 5.—Artist’s concept of internal package in situ. Ceramic box approximately 1 in. × 2 in. × ½ in. lies in a hole in the skull. Five hundred electrode lead wires and the platinum electrodes are in a Dacron net covered with medical silastic rubber. The latter is seen as a pad under the ceramic package and covering the medial surface of the visual cortex (striate cortex or area 17 of Brodmann). The induction coils which are not shown would be in a flat silastic mat to be placed near the skin toward the top of the head. (From Marg et al., 1970b.)

sterilization may react with implant materials (steam sterilization is recommended since chips withstand 125 deg. C. temperatures). 6. Migration of implants may occur.

One consideration in stimulation studies is the need for some way of standardizing the descriptions of sensory experiences. In vision this is fairly simple because the patient can be asked to match his sensory experience with an external spatial arrangement (at least as far as localization is concerned). For the noncongenitally blind it is easy to ask if they see “a figure,” etc. The task is more difficult in hearing, because subjects usually report sounds as “buzzing,” “knocking,” “crickets” (Dobelle et al., 1973), and these are difficult to quantify.
Dobelle's group (1973) found that neither the waveform nor the polarity of stimulation influenced sensory experience. Varying frequency over a range of 25 to 100 Hz and pulse duration from 0.5 to 2.0 msec. likewise had little effect. (Typical stimulation values are 50/sec. pulses, 1.0 msec. duration with a train length of 1 sec.). The only two variables which significantly affected sensory experience were amplitude of the stimulus and localization on the cortex. Changes in the former altered the loudness of the sensation, while changes in the position of stimulation on the cortex altered the pitch of the sound. One important finding was the fact that the stimulation threshold for evoking a sensation (typically 6 ma.) was about double that for visual stimulation. This makes the possibility of tissue damage even more likely.

Because stimulation is to take place over such a long period of time in prosthetic devices, the events which occur at the electrode-tissue interface must be well understood. The paper by Dobelle et al. (1973), contains a good overview of these events, which are summarized below.

Attraction of charges from the electrolyte when the electrode is charged (so-called “double layer” reactions) are not considered a problem since reversal of polarity in biphasic stimulation will cancel this
effect. Sometimes the electrode and electrolyte interact in such a fashion as to result in a residue which remains on the electrode surface ("surface reactions") and may alter its stimulation properties. Even platinum, considered an inert material, is susceptible to these reactions. Although some of these reactions may be reversible, a far more dangerous situation arises when the results of the charged electrode-electrolyte reaction is dispersed in the electrolyte in a fashion which precludes reversibility of effect ("charge transfer reactions"). The chemical complexity of bodily fluids dictates that these factors be taken seriously. Factors such as amplitude, pulse rate, and duration as well as electrode size and material can also affect the rate at which these events can take place, but the single most important factor appears to be the waveform. Specifically, monophasic pulses maximize the probability of all three of the aforementioned events. Biphasic waves are preferred by these authors, although they point out that it is difficult to achieve a waveform in which positive and negative phases are symmetrical (even monitoring it with an oscilloscope risks 2 percent error). To improve a biphasic pulse they recommend leading with the negative phase and capacity coupling.

One way to overcome the problems which arise because of these electrolytic reactions is to use a capacitor electrode such as has been described by Guyton and Hambrecht (1973). It is designed to eliminate the toxic products of oxidation reduction and corrosion which occur in metal electrodes.

The electrode is a small disk made of fused tantalum powder. The result is a porous electrode which is small but has a large surface area. An anodizing process forms tantalum pentoxide over the surface which serves as a dielectric. Electrons cannot pass the insulating barrier but current flow can be effected by attraction and repulsion of ions in the electrolyte to the charged electrode. Guyton and Hambrecht (1973) reported low leakage of electrons with this technique when the electrode is operated at positive potentials.

These electrodes were compared with capacity coupled platinum electrodes in a 6-month chronic stimulation study in monkeys. Both performed similarly and seemed to cause no serious tissue reaction as judged by stability of thresholds over time. One disadvantage of the porous electrode is that organic material may collect in pores and alter the properties of the electrode. Another limitation of the electrode which could prove advantageous is that if the capacitor electrode is charged with a voltage higher than that used to form the dielectric, further tantalum pentoxide will be formed. If enough is formed the electrode will fail, and this is a good fail-safe device to prevent overstimulation of the cortex.
**Heart Stimulation**

The rhythmic activity of a normal heart is controlled by a small area of tissue called the sinoatrial node which lies between the superior vena cava and the right atrium. This tissue sets up an excitatory wave which spreads out rapidly over the atrial musculature. As a result, the atria contract, expelling blood into the ventricles. In the region between atria and ventricles lies another area of tissue which is also specialized for pacing, the atroventricular node. Under normal conditions it acts in coordination with the atrial activity, but it is capable of acting as a reserve pacemaker when sinus activity is suppressed. There is a slight pause before the wave of excitation passes over the junction between atria and ventricles. This enables the atria to complete their systole before excitation spreads to the ventricles. Excitation spreads rapidly over the ventricles, causing them to contract (ventricular systole), which in turn expels blood into the pulmonary artery and aorta. Following this, all chambers are relaxed briefly (diastole).

Artificial cardiac pacing is employed when there is a disturbance of some sort in these coordinated activities. This may come about as a result of alterations in the sinus rhythms, blocking of conduction, or when ectopic pacing develops. The clinical manifestations which dictate the need for pacemakers are tachycardia (excessively rapid heart beat), bradycardia (slowing of the heart rate), cardiac arrest, or fibrillation.

When cardiac pacing is called for either on a temporary or on a permanent basis, there are a number of types of pacemakers to choose from, depending on the nature of cardiac dysfunction. Only implanted electrodes will be considered in this review. The esophageal electrode will be excluded since it is not strictly implanted. The interested reader should consult Rowe et al. (1969) and Burack and Furman (1969) for information concerning this type. In a paper by Keller et al. (1972) the five basic types of pacemakers are presented and compared.

The **fixed-rate** pacemaker is intended to substitute for the heart's inherent rhythm. Its action is to generate pulses at regular intervals, usually about 70 beats per sec., regardless of whether the heart beats by itself. Its simple circuitry, reflecting its simple function, makes it a highly reliable system; however, its independence of heart activity represents a hazard in the case of resumption of heart functioning. Impulse competition and fibrillation could result, with possible lethal consequences. It is, therefore, the preferred technique only in cases of sinus arrest or atrophicventricular (A-V) block.

The purpose of the **P-wave synchronous** pacemaker is to sense the activity of the sinus beat (P-wave), amplify it, and (after an electronic
delay, mimicking normal A-V delay) pace the ventricle. It is used in cases where the sinus is functioning to some degree, but A-V conduction is blocked. Its rate, then, is controlled by the sinus rate, but circuit design protects the device from abnormally high pacing rates such as occur in tachycardia. The design also prevents triggering by other electrical activity of the heart (such as the large R-wave associated with ventricular depolarization). In cases where there is no sinus beat (sinus arrest), the device functions as a fixed-rate pacer. Should normal A-V conduction resume, there may be impulse competition with A-V pulses and pacemaker-initiated pulses arriving at the same time.

Both the fixed-rate and P-wave synchronous pacemakers run the risk of impulse competition. In cases where normal heart functioning is intermittent a demand pacemaker is advisable. There are two major types, the demand/standby, R-synchronous pacemaker and the demand/standby, R-inhibited pacemaker.

In the demand/standby, R-synchronous pacemaker system, a single lead is placed in the ventricle for both detecting and stimulating functions. The device is capable of sensing the R-wave (associated with ventricular contraction), and all other signals are filtered out. If no spontaneous ventricular activity is present, the unit functions as a fixed-rate pacemaker. If an R-wave does appear, the device is triggered to send out its pulse synchronous with the heart's natural activity.

The demand/standby, R-inhibited pacemaker functions like the R-synchronous unit with the exception that the R-wave signals the pacemaking impulse to be inhibited, allowing the ventricle to function on its own. The pacemaker substitutes for missed beats nevertheless.

The sequential A-V pacemaker is for temporary pacing, with the circuitry, therefore, remaining external. The device stimulates both atrial and ventricular contraction and is inhibited by spontaneous ventricular beats.

The Keller et al. (1972) paper contains more detail concerning the engineering requirements of these pacemakers, should the reader be interested. In choosing among these devices, the clinician should consider that demand pacers involve more complex circuitry and, therefore, introduce the problems of added cost, increased chance of failure, and greater battery demands. The R-inhibited pacemaker does present some savings in the latter respect. The more complex the circuitry, the greater the chance of interference. Picking up extraneous signals can be more dangerous for P- and R-wave synchronous devices since they can misinterpret the signal as heart activity and pace the heart at an excessively high rate. In the R-inhibited type, the device can be prevented from pacing by an extraneous signal which is a problem in cases where there is no inherent rhythm. Finally, the more complicated the circuitry, the greater the chances of failure, which again can be serious when the
heart is incapable of any activity on its own.

There are many techniques for implanting pacemaker electrodes in the heart, but the first decision to be made is whether to implant the leads under general anesthesia, employing thoracotomy, or whether to insert them by venous route (through the skin), which can be done under local anesthesia. Since heart disease is generally debilitating and also tends to occur in the elderly, the latter choice is the one often made. Nevertheless, refinements have been made in thoracotomy, such as using a parasternal or substernal extrapleural approach, making this the safer and still preferred technique of those such as Frank and Zoll (1969).

Other nonthoracotomy techniques have also been tried: Dixon et al. (1972), an extrapleural transmediastinal approach; Carlens et al. (1965), a superior mediastinal approach; and Behrends et al. (1966) and Smyth et al. (1967), a subxiphoid approach. The advantage of a surgical technique is that placement is exact with little danger of heart puncture. It is almost an essential technique if myocardial placement (i.e., attachment to heart muscle) is desired, although Bleifeld et al. (1972) and Schaldach (1971) have developed transvenous electrode tips with tiny hooks to fix the electrode in cardiac muscle. (Usually myocardial attachment is done with sutures.) The chief risk with a major surgery technique is the surgical mortality rate.

Dixon and colleagues (1972) claim comparable morbidity with transvenous and transmediastinal techniques. Once implanted, myocardial electrodes show minimal tissue reaction (including both heart and artery damage), are less often displaced, and show little change in threshold (Frank and Zoll, 1969). It should be noted that proper looping and anchoring of leads is required in order to prevent undue stress on the sutures.

Nevertheless, the frequent choice nowadays for both temporary and permanent pacing is percutaneous, transvenous insertion. A variety of routes have been chosen including the femoral, subclavian, basilic, jugular, and cephalic veins. The destination is either the atrium for atrial sensing (as in P-wave synchronous pacing) or pacing (for bradycardia), or the apex of the right ventricle for sensing or pacing. In order for placement to be accurate, one or more methods of monitoring insertion must be used. Fluoroscopic and X-ray guidance has been most common, although Nelson et al. (1970) point out the necessity of X-rays in more than one plane. Each type of pacemaker seems to have a standard stimulus threshold which indicates the ventricle has been “captured” for successful pacing. Endocardial electrocardiograms, obtained from the electrodes as they are inserted, have also been used to locate electrode tips (e.g., Cagin et al., 1972). When successful placement was achieved the EKG showed large ventricular complexes and a slight trace eleva-
tion, the so-called current of injury, when the tip contacted the endocardium.

Some of these techniques have been modified for quick insertion for emergency, temporary pacing. One method requires no movement of the patient and minimal monitoring equipment is to insert electrode catheters percutaneously through the subclavian vein, using only intraventricular EKG to monitor placement. Although effective for emergency situations, chronic obstructive pulmonary diseases can contraindicate this subclavian approach. There is also danger of pneumothorax and air embolism with this method. Furthermore, a comparison of a fluoroscopically guided femoral technique with the subclavian technique over a 72-hour period (Cagin et al., 1972) showed more electrode displacements in the latter case.

Schnitzler and Damato (1972) proposed a “floating” balloon catheter electrode to speed up insertion in temporary transvenous ventricular pacing. A catheter is introduced through the basilic vein and advanced until it reaches the level of the great veins whereupon it is inflated with 1 cc. of air and then “floated” into position. The balloon is then deflated before the electrode tip comes to rest in its final position. Average placement time is 2 minutes.

In cases of temporary pacing, the stimulator is generally placed outside the body. Procedures involved in permanent implantation of stimulus generators can safely be carried out with the temporary system operating.

The generator unit is usually implanted in subcutaneous pockets in the pectoral region. Green et al. (1972) found that the tendency for these units to migrate posteriorly from the axilla can be prevented if they are implanted, instead, behind the pectoralis major.

In order to decide which type of pacemaker package to use, one has to consider the effect each type can have on the patient. A perfect pacemaker unit is worthless if it cannot be inserted properly, does not stand the test of time, or is simply dangerous to the patient.

Many kinds of complications have arisen with pacemaker insertion. The dangers of thoracotomy have already been mentioned. The dangers in venous insertion involve bleeding and hematoma at the entry site, irritation of the vein, puncture of the vein, puncture of the myocardium, missing of the ventricle or placement in inactive tissue, catheter damage, or breakage, and transient heart arrhythmias produced by either mechanical irritation or the beginning of electrical stimulation.

Certain mechanical problems can develop with long-indwelling catheters. Because the patient is a moving organism, there is always a danger of stress fractures and dislodgement or migration of the lead or tips. There is a susceptibility to infection anywhere along the course of
the catheter and the tips also seem susceptible to thrombosis and fibrous encapsulation.

Some specific cases are worth mentioning as potential long-term dangers. Nelson et al. (1970) documented three unusual cases. In one case, too much catheter was pushed in, resulting in buckling of the catheter, which, when the patient was recumbent, resulted in a loop extending into the right atrium. This buckling when prone dislodged the tip from the ventricle surface, resulting in failure of pacing. Presumably, the excessive length also increased the chances of myocardial perforation. In a second patient, even though the catheter insertion was fluoroscopically monitored, placement was in a posterior coronary vein, which could only be detected by X-ray in another plane. This problem demonstrates the need for three-dimensional assessment of tip location. A third patient was in the habit of rubbing lubricating cream on her incisional scar. This caused the electrode leads to “reel in” by winding around the generator unit. As a result, the pacemaker tip was withdrawn into the superior vena cava where it stimulated the right phrenic nerve, causing hiccups. This occurred even though the catheter was supposedly anchored during surgery.

Sidd et al. (1969) also reported a case of catheter buckling. The tip was fixed in the right ventricle but the electrode had formed a loop which protruded through the pulmonic valve and on into the pulmonary artery. The loop produced a thrombosis which extended into the branch artery serving the lower lobe of the lung. The patient died.

Becker et al. (1972) presented three cases of thrombosis and fibrous encapsulation, pointing out the potential dangers that an indwelling catheter can produce. On a short-term basis they found the catheter to be encased in a thrombotic shield and found a superficial mural thrombosis in the superior vena cava at the right atrial junction. On a long-term basis, fibrous encapsulation tended to appear at the superior vena caval-right atrial junction, at the tip of the catheter at the apex of the right ventricle, and in one case near the inferior vena cava and coronary sinus. If an attempt were to be made to remove these leads, serious complications could result.

Green et al. (1972) reported pacemaker migration. In one case the catheter extruded through the neck, and in two cases the generator migrated posteriorly from the axilla. Most cases of electrode migration simply involve displacement of the tip by a small amount, rendering it nonfunctional.

Though these complications are relatively rare, their mere existence indicates caution in future pacemaker implantations. Further discussion of complications of insertion can be found in Lown and Kosowsky (1970).
In order to have a useful and efficient system, it is important to take into account the electrode leads, the stimulus pulse generator, and the point of contact between the electrode and the heart.

In discussing electrode leads, two major factors are to be considered: monopolar vs. bipolar stimulation and the physical properties of the leads.

All stimulation is, of course, bipolar; only the return paths for current differ. For bipolar leads, both are usually contained in a single catheter and are, therefore, more convenient for emergency procedures. In a monopolar arrangement, charge usually returns to the generator housing in a diffuse path through the body. (A bipolar system can be converted to a monopolar one if a lead breaks.) Because large, indifferent electrodes in monopolar systems have such low resistance, there is about 50 percent saving in battery energy (Keller et al., 1972).

The requirements of the leads are that they be made of nontoxic materials, and that they be flexible and strong enough to withstand the stress both of cardiac and body movements. Transvenous electrodes must, in addition, be able to withstand the stress of insertion as well as be able to flex at the appropriate points.

Flexibility has been achieved easily by the use of coiled electrode leads. A removable stylet, inserted through the central canal, can provide the requisite stiffness for insertion. The leads are then usually housed with a nontoxic tubing such as silastic.

Clinical evidence seems to indicate satisfactory durability for most kinds of electrode leads, the leads usually outlasting the generators. Green et al. (1972) for instance, using three types of Medtronic bipolar catheters, reported leads lasting up to 58 months, compared to a 2- to 3-year lifespan of generators.

The entire pacemaker system, should, of course, be pretested before insertion into the patient. Stress due to surgical implant and patient activity and presumably other unknown factors, nevertheless, can cause dysfunction of one or both of the leads. Green et al. (1972) discussed what can occur in such cases. In a bipolar stimulating system, a variety of things can happen. Should the insulation fail on one of the bipolar leads or the conduction wire and insulation break at the same point, an alternate pathway for conduction can occur, but the pacemaker will continue to function. Fracture of both conductors and insulation at the same place will result in a short circuit and consequent pacemaker failure. If the conducting wire within the insulation fractures, resistance will increase, which in turn will reduce the current to the heart muscle. Failure to pace the heart will result, although there may be intermittent functioning of the pacemaker as the two fractured ends make contact. It is possible that increasing the voltage might overcome this increased resistance, but some generators do not have high voltage capacity. In the
first two cases, lead failure would probably only be diagnosed in a routine checking, whereas in the latter two, clinical symptoms of missing pacing would be evident.

Fracture of a sensor lead in a demand pacemaker system also presents a serious problem, as reported by Nevins et al. (1971). Although tested before and monitored during surgery, a demand pacemaker showed intermittent failure especially during patient movement. Upon removal from the patient, it was found that only during agitation of the catheter could the increased resistance be detected (10,000-20,000 ohms as compared with normal resistance of 5 ohms). For the catheter used in their patients (Electrode No. 5651, U.S. Catheter and Instrument Co.), fractures were most common at the junction of the terminal pin and proximal catheter limb. The repair was simply to make the system unipolar by introducing a subcutaneous anode. They suggested that tension could be reduced at this point either by making a large loop in the external part of the catheter or by using an adaptor plug or cable at the junction. If the fracture had occurred in the stimulating cable, the Medtronic 5840 generator would have been capable of overcoming the extra resistance. The heart output, however, is small and constant and was, therefore, incapable of overcoming the increased cable resistance.

Repair of pacemaker leads can be accomplished by withdrawal and replacement. Some, however, have been able to repair leads in situ (Chua et al., 1971; Parsonnet et al., 1963; Zoll et al., 1961; Rainer and Dosch, 1964).

In discussing pacemaker generator units the engineering considerations for a pacemaker generator system will not be dealt with, since different metals, wire length, and tip type will dictate different power needs and since different types of pacemakers will require different circuitry. Suffice it to say that the unit must generate enough energy to cause the appropriate changes to occur at the electrode-heart interface and that these needs will be discussed in the interface section. Keller et al. (1972), van Heeckeren et al. (1969) and Bowers (1969) present more information regarding engineering aspects of pacemakers.

The interest of this paper lies in the problems which can occur with the pacemaker once it has been implanted. Specifically, these problems concern interference with and failure of pacemaker function.

In any pacemaker which depends, for proper functioning, on the sensing of heart activity (such as P- or R-wave sensors), there exists the possibility of sensing extraneous electrical activity. This activity may stem from other internal physiological activity such as a high T-wave (Cheng et al., 1971) or may come from sources outside the body such as auto ignition systems, electrocautery units, radio frequency transmitters, radar transmitters, physiotherapy diathermy units, electric razors, and microwave ovens (Titel and El Etr, 1968; King et al., 1970; Yatteau,
Most of these present transient or only light interference, as have electroshock therapy (Youmans et al., 1972) and airport weapon detectors (Smyth et al., 1972). Michaelson and Moss (1971), suggested that most of these problems can be overcome by proper shielding of pacemaker circuitry. Widmann et al. (1972) also noted that when a temporary pacing electrode is left in place for emergencies following permanent pacer implantation, the tips are sometimes touching. The resultant friction can set up enough activity to be sensed in a demand pacer as heart activity, thus causing the pacemaker to miss a beat. When this was found the temporary electrode was simply repositioned by a small amount.

The most serious problem facing a pacemaker patient is failure of the pulse generator. Although miniature circuits require little energy and the zinc-mercury oxide batteries which are frequently used have long life, there is nevertheless no such thing as a true permanent pacer. At various intervals of time, the unit must be deplanted and the batteries or whole unit replaced. A major question arises, then, as to when to deplant the device. This decision must be based on the predicted life of the unit and the consequences to the patient if generator failure occurs.

Green et al. (1972) tested several types of Medtronic pacemakers, including fixed-rate generators, demand generators, and redundant cell types. The longest that any lasted was 3 years. They point out that some suggest replacement of the generator after a fixed, safe amount of time, e.g., Chardack, who claims only 10 percent failure rate if pacemaker generators are routinely replaced every 18 months. Green et al. (1972), however, argued that surgery is traumatic, expensive, and occupies a great expenditure of hospital time and space. Therefore, they felt that it would be far better to closely monitor pacemaker functioning, since it is possible to detect a deteriorating instrument. Generally, rate increases and voltage output decreases as the generator winds down. A number of techniques for monitoring the functioning of implanted pacemakers have already been tried (e.g., Schmutzer, 1969; Ryden and Thorander, 1970).

Clearly, however, the final decision for replacement rests with the patient. Failure of a fixed-rate pacer in a patient with no endogenous heart rhythm would be fatal (and indeed such a case was documented by Green et al., 1972). Failure of a demand pacer unit is not quite as serious, however, since the patient usually has some normal rhythm. If the pacer speeds up, he has a faster rate and perhaps has competitive pacing; should it slow, he will revert to original symptoms. Likewise, a voltage drop would result in failure to pace and reversion to original symptoms.

Yet another consideration is the nature of the electrode proper. The myocardial electrode tip as presented by Greatbatch and Chardack (1968; see Fig. 7) was merely the terminal turns of the helical platinum-
iridium wire of which the leads were made. Thus, there were no potential junctional problems between tip and leads. Platinum was chosen for its inertness and the iridium added tensile strength. The last few turns were spread a little so that tissue could flow between them to help secure the tip. A solid platinum-iridium core was used for reinforcement. The electrode tip was held in place by means of sutures.

The same authors also introduced an endocardiac model (see Fig. 8). A bipole system was used with both leads being housed in separate lumina of the same silastic sleeve. The leads were coiled stainless steel, with one tip welded to the rounded platinum tip of the catheter, and the other to a platinum ring just posterior to the catheter tip. Removable stainless steel stylets provided structural support during insertion. Fibrous tissue held the tip in place in the right ventricular apex.

The performance of these electrodes seemed to be good. Thresholds for the myocardial electrodes were relatively low (1.5 to 2.5 ma.) and were reported stable for up to 5 years. No inordinate tissue reaction was observed. Thresholds for endocardiac electrodes were generally higher and more variable. Presumably this was because the contact of the tip with tissue was less certain.

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**Figure 7.**—Diagram of platinum coil myocardial electrode. Distal third of the tip of the coil is bare and is placed into depth of myocardium. The terminal three turns are slightly spread to facilitate ingrowth of tissue. The reinforcing core extends into the bare portion of the coil tip. (From Greatbatch and Chardack, 1968.)
Threshold undoubtedly depends upon the particular electrode used and the method of fixing it to the heart. Overdijk and Dekker (1969), using different endocardial and epicardial electrodes than Greatbatch and Chardack (1968), found that after 11 to 21 months of implantation, endocardial electrodes had slightly lower thresholds than epicardial.

As previously discussed, one of the major hindrances to pacemaker operation is the short life of the batteries. It is reasoned that if the energy needs for the whole system can be reduced, the batteries will last longer. Very little change (about 30 to 50 mv.; Keller et al., 1972) in resting potential is required to effect cardiac depolarization. In order to accomplish this with a pacemaker device, however, a relatively great deal of energy must be expended. This is partly because of the energy required to deliver charge from the battery all the way to the electrode tip, and partly because of the impediments to charge transfer at the electrode tip (e.g., polarization, electrolytic activities, edema, placement of the electrode in nonmuscular tissue, etc.).

The major problem with Greatbatch and Chardack's (1968) electrodes and any similar electrodes lies in the fact that with passage of current they become polarized. Greatbatch and Chardack (1968) were able to demonstrate that this is responsible for most of the voltage loss in cardiac electrodes. In a standard metal electrode with bare surface exposed, any attempt to decrease the energy requirement by reducing electrode size or stimulus duration has a side effect of increasing polarization, which in turn requires more energy to overcome in order to maintain constant current. Increasing current density in this manner may have the effect of corroding the metal.

To solve this problem a number of new electrode designs have been offered. Parsonnet et al. (1968) have designed a differential current density (DCD) electrode (see Fig. 9) which consists of a small chamber filled with an electrolyte. The conducting wires which terminate in the chamber were made of Elgiloy flattened and coiled in helical fashion so as to increase surface area. A tiny hole in the tip of the chamber served as the point of contact with the heart muscle. The net effect resulted in low

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**Figure 8.**—Diagram of construction detail of the tip and contact points of the Chardack endocardial electrode. (From Greatbatch and Chardack, 1968.)
current density at the metal (hence no corrosion or polarization) and high current density at the small hole where contact is made. They implanted an endocardial model in seven human subjects and not only was successful pacing achieved, but also the energy requirements were 10 to 20 times lower than in standard metal endocardial electrodes.

Schaldach. New pacemaker electrodes

![Figure 9](image.png)

**Figure 9.**—Dimensional drawing of the DCD electrode. (From Schaldach, 1971.)

The potential problem with this type of model stems from the fact that any foreign body inserted in human tissue has the potential of stimulating thrombosis (blood clots) and fibrous tissue growth (the body's defense attempt to encapsulate and isolate the foreign body). Even though materials and techniques are carefully chosen to minimize these reactions, they represent real problems. In the case of the Parsonnet et al. (1968) electrode, any invasion of the chamber with thrombic or fibrous material would clearly alter its electrical capabilities. They themselves, however, reported that neither of these problems arose in seven patients who had been implanted for up to 94 days.

![Figure 10](image.png)

**Figure 10.**—A thin dielectric layer is used on the surface of a metallic electrode tip. (From Schaldach, 1971.)
Nevertheless, the possibility exists for this to occur, so Schaldach (1971) has offered another design (see Fig. 10). His electrode also uses helical Elgiloy wire as conductors to and from the generator unit. The tip is housed in silastic except for the exposed metal surface. The major advancement over earlier models, however, is that the exposed tip is coated with a dielectric material (electrochemically deposited tantalium dioxide). The net effect is that the electrical charge can pass through the interface but no electrode corrosion, gas formation, or metabolite reactions can take place. Clinical testing in five patients indeed demonstrated that no electrochemical reactions occurred, capacitance remained stable, and further this was done with one-third the energy required with standard metal electrodes of similar size. Only a thin fibrotic layer was observed. Although it requires more energy than the Parsonnet et al. (1968) design, it would see to be more advantageous in that it provides safer contact with tissue and probably represents a more reliable instrument.

**Dorsal Column Stimulation for the Relief of Pain**

In cases of terminal cancer, amputation, or spinal or neural injuries there occurs a type of pain which is constant and unbearable without some form of therapy. In the past, the treatment has been almost as debilitating as the symptoms: drug therapy may produce addiction and surgical intervention (cordotomy, commissurotomy, rhizotomy, lobotomy and thalamectomy) is dangerous. Sometimes this type of treatment produces only partial or temporary relief and involves unwanted side effects such as loss of muscle tone, altered sensory processes, or impairment of vegetative functions.

Two major electrostimulation techniques have been offered as alternatives for the relief of pain. One involves stimulation of peripheral nerves; the other involves stimulation of the dorsal columns in the spinal cord. The first technique was initiated by Wall and Sweet in 1967 and simply involves stimulation of sensory nerves or roots supplying the painful area. The patient’s pain is thereby masked by a “tingling” sensation. This technique is similar to techniques covered in the section on nerve stimulating electrodes. The more complex technique of stimulating the dorsal columns will be considered here.

The technique was first suggested by Shealy et al. (1967) and was based on the “gate theory” of Melzack and Wall (1965) which states that stimulation of large-diameter myelinated (cutaneous, fast-conducting) fibers will inhibit the slower, unmyelinated (pain) fibers. It is believed that the site of this inhibition is in the substantia gelatinosa of the dorsal horns.

Several similar varieties of electrodes have been used (Shealy et al., 1970; Nashold and Friedman, 1972; Sances et al., 1970). Those used by
Sances and his coworkers consisted of 0.5 mm silver solder balls attached to Teflon-coated stainless steel wires which were placed over the spinal cord and sutured to the dura. The more common procedure, represented by the other two studies (see Fig. 11), was to have small discs or plates of platinum affixed to a strip of silicon-impregnated Dacron mesh. This strip was placed on the spinal cord several spinal segments above the level of pain input. Wire leads ran from the electrodes to the receiver implanted somewhere near the site, and power was delivered by means of an external battery-powered radio transmitter placed over the receiver site (Avery Labs—Nashold and Friedman; Medtronics, Inc.—Shealy, et al.).

The stimulus parameters varied with each study, partly due to electrode configuration and partly due to electrode placement. Nashold and Friedman (1972) used four platinum discs in a bilateral arrangement placed beneath the dura but external to the arachnoid. Shealy et al. (1970) used 5-mm. square plates arranged longitudinally and attached to the dura or placed in the subarachnoid space. Those of Sauces et al. (1970) were placed in a variety of configurations along and around the cord. The best parameters found by Nashold and Friedman (1972) were 0.5 to 3.0 v., 15 to 200 Hz, square wave pulses of 200-µsec. pulse width. Shealy et al. (1970) employed a capacity-coupled biphasic square wave with a pulse duration of 0.5 msec. and voltage ranging from 0.3 to 3.0 v. Patients preferred a frequency in the range of 100 to 200 Hz. Sances et al. (1970) reported best results with 100-Hz, 2-msec. 1-kHz sinusoidal burst currents applied for approximately 30 min. (0.5 to 1.0 ma. cur-
The external transmitter in all cases allowed the patient control over amplitude, pulse duration, and frequency. Spread of current was probably limited fairly well to the dorsal column because any involvement of nearby motor pathways would have produced a notable effect. Nashold and Friedman (1972) found some relief in half their patients; one-fourth had complete relief. Shealy et al. (1970) found that all had some relief; in half it was rated excellent. Sances et al. (1970) reported that all patients had some relief.

Pain relief in most cases was accompanied by a buzzing or vibrating sensation which varied with frequency. This sensation extended to other areas in varying degrees, depending on placement of electrodes and on stimulus parameters. There was a wide variation in the nature of pain relief. For some patients the relief only lasted for the duration of stimulation and therefore required constant stimulation (at least during waking hours, although some could not sleep without it). In others, stimulation of 15 to 60 min. had an aftereffect of from 1 to 5 hours. Nashold and Friedman (1972) reported the most success with burning pain associated with CNS damage, while bone, muscle or joint pain was least affected. Normal sensory and motor function remained intact during stimulation, although Nashold and Friedman (1972) reported some reduction in proprioception. Implants have been in place for up to 3 years. This technique is inadvisable for patients with severe psychiatric disorders, but selection may be a problem since chronic pain understandably can produce depression.

The long-term effects of tissue reaction to the implant proper and to stimulation are still unknown, though Nashold and Friedman (1972) have noted thickening of the arachnoid. A new technique placing the electrodes below the arachnoid appears to have solved this problem. They also noted postoperative motor deficiencies in some patients who were subsequently found to have the electrode array pressing on the cord. The fact that at least one patient has been implanted for 3 years is, however, encouraging. Leakage of CSF was a problem in some patients and appeared to be remedied by more tightly suturing the dura.

Placement location may be an important factor, since Nashold and Friedman (1972) had to reposition a number of their electrodes. It should be noted that there is a layering on of fibers in the longitudinal plane of the dorsal column, with the caudal representation gradually assuming a more medial position in the column. Segmental level of placement and spread of current can also figure in the success of this technique.

A postoperative test of the system at 7 days was incapable of predicting the ultimate success of the procedure. Nashold and Friedman (1972) suggested that one way that failure rate might be reduced is to employ...
the technique of percutaneous stimulation as a screening device prior to implantation (Hosobuchi et al., 1972).

Finally, the most perplexing consideration is that no one is sure how the device works. Perhaps when more is understood about the anatomical factors involved, the device can be refined for greater success.

Nerve Stimulation

Chronic nerve stimulating electrodes have been implanted for a variety of reasons. Sensory nerves have been stimulated for the relief of pain (Wall and Sweet, 1967; Sweet and Wepsic, 1968); the carotid sinus nerve for treatment of hypertension and angina (Schwartz et al., 1967; Braunwald et al., 1967); the phrenic nerve for ventilatory support in quadriplegics and people with lesions in or dysfunction of the respiratory centers (Glenn et al., 1972); and the peroneal nerve to stimulate dorsiflexion to prevent drop foot in hemiplegics (Yergler et al., 1972).

A variety of electrode systems were employed in these studies. Glenn et al. (1972) used a bipolar platinum electrode in a silastic cuff which was
placed around the phrenic nerve. This resembles an electrode described by Dubkin (1970) for use in animals (see Fig. 12) where two wires are wrapped around a Lucite cylinder and inserted in a cuff made of a short piece of flexible tubing. The tubing is slit longitudinally so that it can be clasped around a nerve and is held there by its natural tension. An appropriate cut in the tubing allows for exit of the lead wires. Silastic cement holds the wires in place. The Lucite cylinder might possibly do damage to the nerve, but appropriate modification of the design and selection of materials could make this device adaptable to human use.

Electrodes used by Yergler et al. (1972) were the flattened ends of platinum lead wires (2.5 mm. × 20 mm.) lying inside a silicone-coated dacron flap which was wrapped around the nerve. Implanted receivers and external radio wave transmitters were employed to minimize the possibility of infection.

The purposes of the above studies varied, but information can be gathered from them which is generally applicable to uses of chronic nerve stimulation. The Glenn et al. (1972) study provides information concerning nerve fatigue and nerve damage. The phrenic nerves suffered from fatigue which began to appear after 12 to 18 hours of repeated stimulation. These authors found that after 24 hours of nerve stimulation the diaphragm would contract only half the normal amount. This problem was overcome simply by alternating the stimulation of the left and right phrenic nerves every 12 hours. Each nerve fully recovered within a few hours.

The system has been used successfully in the paraplegic for 14 months and in people with respiratory center damage for up to 3 years. In one patient who died from other causes 22 months after implantation, the phrenic nerve was examined histologically and found to be free of apparent damage. Furthermore, thresholds in the phrenic nerve did not rise much after many months of stimulation. In one patient the threshold did rise severely, followed by diaphragm collapse. This appeared to be caused by the residue of ethylene oxide sterilization. As a result the authors now heat sterilize the nerve cuffs and no further incidence has occurred.

Glenn and colleagues (1972) also point out one particular danger with phrenic nerve stimulation for ventilatory support—the danger of failure of part of the circuitry. It is important to design the system with redundancy and with the capability for automatic switching to stimulation of the other phrenic nerve in the event of such failure.

The Yergler group (1972) was specifically interested in determining which dimension of the stimulus applied to the peroneal nerve (frequency, duration, or amplitude) it would be best to vary in order to better control the lifting of the foot. This information might be useful or other cases of neuroelectric control of movement. Frequency was
found not to be significant in controlling the force of muscle response. Pulse duration was not practical in their situation so they settled on using amplitude to control the force of the response from zero to maximum.

The purpose of the Testerman et al. (1971) study was to determine whether an electrode configuration could be found which would reduce current spread, a factor which was thought to be responsible in carotid nerve stimulation for bilateral auricular pain and tickling or choking in the throat.

A very careful analysis of nerve properties and current flow in a variety of electrode configurations was determined in order to select an arrangement which would excite the nerve but would entail limited spread of current. In vivo testing, however, revealed that an idiosyncratic feature of the carotid sinus nerve rendered the results of stimulation unpredictable. That is, the carotid sinus nerve is not unitary, but rather consists of many separate fibers. To stimulate this "nerve" these fibers had to be drawn together and in the process they were accompanied by a great deal of connective tissue (80 percent of the total bundle). This caused the effective stimulation parameters to vary from trial to trial. Nevertheless, Testerman et al. (1971) observed that with high voltages in a bipolar experiment, throat muscle contractions were evident. These can be abolished by a tripolar arrangement and indeed this was the recommendation of the authors.

**Muscle Stimulation**

Paralysis of skeletal muscle can come about from a variety of causes but when it is due to damage of the spinal cord or peripheral nerve, i.e., when the muscle remains otherwise viable, the possibility exists for direct stimulation of the muscle by implanted devices. The major requirements of such a muscle stimulation system are twofold. First, a good electrode is needed which can be totally implanted, will not cause pain or tissue damage with prolonged use, but will deliver stimuli capable of evoking normal contractions. Second, the complexity of coordinated movement requires a good programming system to reproduce natural patterns of movement.

With respect to this latter requirement, work is already underway to record from the muscles of normal subjects during movements such as walking, in order to obtain a program which can be applied to the same sets of muscles in a paralyzed patient (e.g., Milner et al., 1969). The studies will not be reviewed here. Consideration will be given instead to electrodes and the clinical and electrical factors involved in muscle stimulation.

Electrodes used by a group of researchers at Case Western Reserve University are based on a Caldwell (Caldwell and Reswick, 1967) design.
These are coiled wires made of 304 stainless steel. Their overall diameter is 0.15 mm, and about 10 mm along the length are deinsulated for a recording surface. Their shape was designed to allow them to flex with muscle contractions and relaxations. To stimulate muscle (in cats) unidirectional regulated current, rectangular (“constant current”) pulses 100 µsec. in duration at a frequency of 10 Hz were used, with the coiled electrode always being the cathode. These parameters effected contraction by depolarizing intramuscular nerves (Peckham et al., 1973).

Since muscles will be stimulated repeatedly, consideration must be given to factors which might produce damage or fatigue in the muscle. Mortimer and Gertler (1971) implanted coiled electrodes in cat muscle and stimulated them for 20 consecutive hours using 50 Hz, 100-µsec. duration pulses with currents of 0, 1, 2.5, 7.5, 10, or 15 ma. Only at the last level was any damage detected. In man, good muscle contraction was obtained within a range of 0.5 to 5.0 ma., reaching asymptote at 3 ma. Peckham et al. (1969) found less fatigue with two implanted intramuscular electrodes than with one if the two were activated sequentially, i.e., the stimuli were switched back and forth between the two at frequencies slightly more than one-half the frequency applied to the single electrode. Peckham et al. (1973) also observed the interesting finding that muscles chronically stimulated at low frequencies developed increased resistance to fatigue, although contraction was slowed somewhat.

Vitreous carbon button electrodes have also been investigated as possible electrodes for use in intramuscular stimulation (Gibbons et al., 1972). In vitro studies and in vivo studies (in chronic and acute animals) established that when used as an anode this material was highly unsatisfactory. In the chronic animal stimulation for 96 hours with a monophasic, pulsed current (5 ma.; 0.1 msec. duration; 60 Hz), and in the acute animal stimulation for 1.95 hours with the same parameters except for a 5-msec. pulse duration, slowly produced pitting or flaking of the anode and inflamed tissue in the neighboring area. Used as a cathode, however, the electrode remained intact and almost no tissue change was observed excepting the formation of a fibrous capsule which is typical even of passive implants.

**Electrical stimulation for Bladder Control**

**Voiding**

In certain cases of serious neurological diseases or injury to the spinal cord it is common to find dysfunction of the urinary bladder. A variety of procedures have been used to remedy this situation, including various forms of catheterization or rerouting of the urine. However, catheters carry the risk of infection and surgery is dangerous. An alternative to these procedures has been developed which, although not yet perfected,
does provide the opportunity for voluntary control of voiding. This technique involves the implanting of stimulating electrodes in the bladder.

In order to duplicate the action of the bladder it is necessary to know how it functions normally. Much of what is known about bladder functioning has been gathered together by Bradley et al. (1971). Sensory nerve endings in bladder muscle respond to tension produced by a full bladder. Impulses travel through the spinal cord, probably to the reticular formation, are modulated, and then return to synapses on motor neurons lying in the spinal cord which serve the bladder. Only a small proportion of detrusor muscle cells are innervated; the remaining cells are excited by electrotonic spread of excitation. There is also much overlap in innervation with one axon serving many muscles and one muscle being innervated by many axons. Studies of detrusor motility show a coordinated sequence of contractions and relaxation in the detrusor muscle to expel the urine.

Attempts have been made to effect voiding by stimulation at various points in the complex sequence of events associated with micturition. Spinal implantation appears dangerous and therefore impractical. Stimulation of pelvic detrusor nerves, although effective, results in nerve fibrosis and ultimately nerve failure (Plaid, 1969). The most likely candidate then appears to be direct stimulation of the bladder itself. Although this appears to be an easy task, a number of engineering and clinical problems had to be overcome to obtain the desired result.

Bradley et al. (1971) sought to replicate the coordinated sequence of muscular contraction of the bladder which occurs under natural conditions. To do this they had to stimulate \( \frac{2}{3} \) to \( \frac{3}{4} \) of the muscle tissue with electrodes that would be flexible enough not to dislodge with the collapsing and refilling of the bladder. This was accomplished by a design using multistranded platinum-iridium wire arranged in helical design and insulated with nylon suture (see Fig. 13). The wires were actually spaced 1 mm. apart and the whole electrode was 2 cm. long. A number of these were imbricated in the muscular wall of the bladder and could be stimulated in any desired pattern (see Fig. 14). The stimulus parameters used were biphasic pulses, 10 to 40 per sec., lasting 0.1 to 5 msec., with current density 3 to 5 ma./cm.\(^2\). A properly timed sequence of stimulating the electrodes was capable of imitating the normal voiding pattern.

A volume sensor was also implanted. It was found to be necessary because if the bladder is too greatly distended not only is there a risk of permanent damage, but also the stretching could separate the smooth muscle fibers which would reduce the possibility of electrotonic spread of current. The sensory receiver and stimulus transmitters were located outside the anterior abdominal wall.

Certain patients are not suitable for bladder stimulation. These are
patients whose bladder muscle is nonfunctional either through damage due to disease or through overdistension. Careful screening of patients therefore required to assess the physical state of the bladder.

A number of complications arose in the design of the electrode. Spread of current was noted to cause urethral occlusion and in some cases pain. Careful design of the electrode and, in certain cases, selective sectioning of neighboring nerves was found to eliminate the problem.

Several other similar techniques have been used, with varying degrees of success. Alexander and Rowan (1972) implanted two pairs of stainless steel loop electrodes on the fundus of the bladder. Stimulus parameters were rectangular pulses of 1 msec. duration, 20 pulses per sec., at 5
to 10 v. The receiver stimulator was implanted and activated by radio transmitter. Improvement was noted in all cases except where the bladder neck seemed dysfunctional.

Halverstadt (1971) reported eight cases in which a commercial AVCO physiological stimulator was implanted. The electrodes were stainless steel wires sewn directly into the detrusor muscle. Although four of the eight cases were considered successful, with one still functioning after 4½ years, a number of complications developed. The most common complication was displacement of the lead wires. Lead wires became detached and migrated through the abdominal or bladder walls. The author suggested that tailoring the unit to suit the patient might help. A second major problem was the incidence of pain, often accompanied by adductor thigh muscle contractions; both problems were likely due to current spread. Relocation of the leads helped in one case. Current spread appeared also to be the cause in cases where there was abdominal or peroneal pain; defecation sensations; spasms in the leg, pelvis, or external sphincter muscles; and erection and ejaculation. It would appear that Bradley's multiple, limited-current electrodes provide a better means of exciting the bladder.

Other complications included breaking of leads which led to hyperdistension of the bladder, rendering it unresponsive to later stimulation. In
another case insulation failed, causing tissue reaction and excessive current spread which caused pain. Finally, the author cautions that laboratory experiments have shown that repeated stimulation leads to a refractory detrusor muscle, even though this does not seem to be a problem in the 4½ year implant.

**Continence**

Caldwell (1967) was able to achieve urinary continence in patients by stimulation of the sphincter muscle involved. An interesting technique which has been developed (Hopkinson and Lightwood, 1966) appears to be a worthy alternative since it does not require a surgical implant and in some cases has long-range remedial effects. The device is actually an intra-anal electrode developed for use in anal-incontinent patients but which was also found to improve urinary continence.

The electrode basically is hourglass shaped, designed so the neck is clasped by the anal sphincter. In cases of rectal damage, the device can be inserted in the female vagina. Two parallel ring-shaped stainless steel electrodes are fixed in the Plexiglas plug so that they lie 1 cm. apart above and below the neck. Stimulation is with biphasic pulses of 1 msec. duration, with a frequency range of 20 to 200 Hz and a maximum amplitude of 25 v. (Higher amplitudes will cause pain.) Several commercial brands are available (Devices, Ltd., and Cardiac Recorders), and each company offers four or five sizes of plugs for different-sized patients (see Fig. 15). Each is powered by batteries which have to be changed every 3 to 14 days depending on usage.

The success of the anal plug may be partly due to the spread of current because the voltages are so high, but certainly a major factor in its success appears to be the training of the pelvic floor muscles. This training occurs partly as a result of the electrical stimulation, partly because of the increased sensory awareness of the area, and partly because of exercises prescribed by the doctors. As a result, many patients showed considerable improvement in less than a year, and some discontinued the use of the device altogether. The technique has been found successful over a wide age range (from 3 to 77 years old) and for a variety of ailments, including rectal prolapse and aftereffects of urological, gynecological, or neurological surgery (Hopkinson, 1972; Glen, 1971). On the other hand, it has been found inadvisable or unsuccessful in cases of urinary infection, high residual urine volume, and spinal cord injury where muscle control is precluded. In some cases the technique fails because the patient cannot walk with the plug in place. Despite these limitations, its safety and simplicity make it a welcome alternative to the surgical procedures described earlier, most of which have a high failure rate due to lead breakage.
FIGURE 15.—The small portable electrical stimulator and range of five plugs to fit most patients. (From Hopkinson, 1972.)

**LESIONING**

The object of this review is to present information dealing with chronic implantation of electrodes in humans. Although lesioning electrodes do not usually fall within this category, a section is included here for the simple reason that the use of stimulating electrodes (and sometimes recording electrodes) quite likely produces some degree of damage to tissue over and above mechanical trauma. In order to prevent this, it is necessary to have a full understanding of how lesions may be produced.

No attempt will be made to review all the techniques for producing lesions. Rather, emphasis will be placed on the variables which affect lesion size. Only lesions of neural tissue will be considered, though most of what is said would apply to other types of tissue. Because neural tissue is essentially nonregenerative, the decision to destroy or remove por-
tions of it in humans should not be taken lightly. The main use of brain lesions so far has been for relief from intractable pain, Parkinson’s tremor, epilepsy, and certain “incurable” mental illnesses.

Early forms of corrective neurosurgery involved either gross extirpations or the severing of fiber tracts with a knife. Such techniques often proved to be unsatisfactory because not only was healthy tissue destroyed in the process, but also blood vessels could be severed which would compound the damage. It was reasoned that highly localized lesions restricted only to the area responsible for the problem would be a much preferred technique. Omitting for the time being the problem of localizing the brain site responsible for the nervous disorder (which lies outside the scope of this review), the task of placing a lesion of exact size has turned out to be a formidable one. It is not sufficient to understand the electrical variables involved, for the tissue itself and its reactions with the electrode and current can contribute a great deal to the variability of lesion size. Since in humans there are many cases of both lesioning and stimulation where little, if any, histological verification is obtained, it is important to learn as much as possible about the effects of current on tissue before the switches are turned on.

A number of techniques have been employed to produce lesions, involving the use of d.c. electrolytic lesion-makers, radio frequency devices based on heat production, and cryoprobes which use the principle of hypothermia. Only the probes involving the passage of current will be considered because, as was mentioned earlier, the aim is to relate lesioning to stimulating electrodes.

A dismal picture was painted by Sweet and Mark (1953) concerning the ability to create by choice lesions of particular sizes. They pointed out that while neurophysiologists tended to follow a “rule of thumb” suggested by Horsley and Clarke (1908) relating size of lesion to strength of current for a given duration, in fact there are repeated instances in the literature of unpredictability of lesion size with fixed stimulation parameters.

Sweet and Mark had become suspicious of their own techniques in placing lesions in human bulbar or mesencephalic areas for the relief of pain. The electrodes they had used were nichrome #20-gauge wire, exposed only 1 mm. at the tip. Electrode arrangement was unipolar, and the implanted electrode was designated the anode to avoid the effects of gas formation which occurs at a cathode in electrolyte. It was also believed that the steady d.c. current would coagulate not only adjacent neural tissue but local blood vessels as well. The 3-ma. current used was always monitored.

The patients were awake so that the effects of lesioning (analgesia) could be monitored. When successful, the duration of each lesioning current varied (1 to 3 min.) as did the total lesioning time (5.5 to 12 min.);
sometimes the electrode had to be repositioned to obtain the desired effect. Although error of placement due to individual differences could account for these results, some strange findings were observed. Variable states of analgesia were obtained and on occasion there was even a lag in the appearance of the analgesia (the next day). Sometimes the duration of stimulation was lengthened but there was no behavioral evidence that it increased the size of the lesion. The size of the lesion varied quite a bit, too, and included one patient with a massive hemorrhagic lesion centered where the electrode had been. Furthermore, attempts to preview the effect of the lesion by passing square-wave current (30/sec.; 1 msec. duration; 2 to 5 v.) were unsuccessful.

Because histological feedback was needed, the authors turned to animal (dog and cat) experiments to try to standardize techniques. To examine the effects of current flow, stainless steel electrodes were used because they deposit iron which can be traced histologically. Lesions were placed in white matter because of the large volume of tissue available and because there are fewer blood vessels. Twenty-gauge stainless steel electrodes with 1 mm. tip exposed were used. A constant current of 1 to 5 ma. was delivered with gradual onset and offset for 10 sec. to 4 min. duration.

The results, as mentioned earlier, were discouraging. There was variability in the size of lesions in all cases, more so with long durations. Current would flow down blood vessels and sometimes cause hemorrhage which further magnified the effect of current. Even avascular areas contained lesions of various sizes. What was more perplexing was that the amount of iron deposited was not necessarily correlated with lesion size.

Since this study was done, a number of good papers have carefully sorted out factors which can affect lesion size. These factors include not only electrical variables but also tissue variables. Although the precise geometrical detail of a lesion cannot now be predetermined, it is possible to control lesion size within a certain range. The variables which affect lesion size will be dealt with in two major sections: electrolytic lesions (d.c. and low-frequency a.c.) and radio-frequency (high-frequency) lesions.

**Electrolytic Lesions**

In using continuous direct current to make lesions, it was noted as early as 1908 (Horsley and Clarke) that more mechanical destruction of tissue occurred at the cathode than at the anode, due to the electrolytic liberation of gas bubbles. This observation has been repeatedly confirmed (e.g., Rowland et al., 1960). Subsequent considerations will argue that neither anodic nor cathodic lesioning techniques (i.e., any continu-
ous unidirectional current) is advisable because of the inability to perform discrete lesions. Nevertheless, if one is forced to choose between the two, anodic produces the more discrete lesion.

It might be speculated that an interrupted current might do less damage than continuous current; that is, the tissue might recover from damage between pulses. In comparing interrupted and continuous direct current stimulation of tissue, MacIntyre et al. (1959) varied both pulse width and pulse interval over a wide range and found that the one critical variable which determined lesion size was the number of milli-coulombs delivered.

It appears that a great deal of the potential damage that can be done by a unidirectional current can be prevented by following it with a current of reversed polarity (e.g., Lilly, 1961; MacIntyre et al., 1959; Rowland et al., 1960). This was studied in some detail by Rowland et al. (1960). Using a square-wave biphasic current, they varied the amount of time polarity was reversed, the frequency of polarity reversal, the effect of a delay between the two phases (up to 150 msec.), the effect of different waveforms, and the number of pulses per train. Comparing monophasic with biphasic pulses, the same total coulombs with half passed one way and half the other produces a much smaller lesion than if the current all passed in one direction. If the two phases are unequal, then less “protection” from damage is afforded as the second phase is decreased.

When biphasic pulses are used to perform tissue lesions, the critical variable (as with unidirectional current) appears to be total coulombs delivered. In the above study it was found that lesion size increased as the number of µC. per pulse increased and as the number of such pulses in a train increased. All other variables were important only insofar as they varied these factors. An important observation, however, was that the above statements were limited by a threshold value. Specifically, if the charge per pulse fell below 20 µC, long trains of pulses accumulating up to 10 total C could be applied without any noticeable tissue damage. Anything above 20 to 25 µC per pulse sharply increased lesion size, reaching a plateau at 300 to 400 µC per pulse. It should be noted, however, that damage was assessed in terms of gross observation. In the light of present-day advanced techniques it is possible that slight damage could have been demonstrated at the lower levels.

What, then, is happening at the anode and cathode and why does reversing the polarity protect the tissue to a certain extent? Briefly, lesions may be produced by the ionic events (including chemical exchanges and thermal and gaseous byproducts) which occur when current is passed, or they may result from the electrical field effects. It was believed by Rowland et al. (1960) that gases released at the cathode cause mechanical damage and that metallic deposits are the substances which
cause tissue irritation and death. When brief current is passed, and then immediately reversed, the chemical processes are also reversed and the tissue is thereby protected from damage. The evidence they presented seems to support their arguments. Perhaps the most dramatic evidence is that when a copper electrode used as an anode is placed in a new area of the brain, it produces a lesion without the passage of current. Furthermore, this effect can be greatly reduced if current is passed so that the wire then functions as a cathode instead. They also found that a biphasic pulse passed through a single wire causes less damage than monophasic pulses of opposite polarity passed through two closely spaced wires. This finding seems to present an argument against the theory that field effects are responsible for current damage. Evidence from the Rowland et al. (1960) paper is especially useful in helping establish “safe” stimulating parameters of waveform and charge.

Since most points concerning electrode variables have already been covered in the section on stimulation, only brief mention of them will be given here as a review.

Electrodes should be as small as possible to avoid tissue trauma during insertion. Blunt tips help push aside blood vessels to prevent hemorrhaging (a major source of lesion variability). It is also helpful to have a flexible electrode that will “give” in the face of tissue (or blood vessel) resistance and move with slight brain movements to avoid the “cheesecutter” effect. Electrode materials must also be carefully chosen so that they can carry large lesioning currents but will not produce toxic reactions with tissues. Tips of fine stainless steel wires have been observed to dissolve with currents of coagulation strength (Loucks et al., 1959). Silver, chlorided silver, and copper metals are especially toxic; noble metals (e.g., platinum, gold) and also stainless steel are less so. For mechanical, toxic, and electrical properties, Crow and Cooper (1972/1973) have found gold wires most appropriate. Most insulation materials are nontoxic, but some will peel off during the passage of large currents. Brudzyński (1971), for example, noted that over time his Bakelite insulation began deteriorating. As well, his stainless steel 0.3-mm. diameter electrode darkened, the surface roughened, and the diameter became smaller so that after 500 mC had been passed through it, its lesion-producing properties were altered.

Another factor of great importance is the amount of electrode tip exposed. It is this factor which (in interaction with stimulation parameters) determines the concentration of charges at the electrode-tissue interface. This variable was explored in a paper by Brudzyński (1971). Stainless steel electrodes, 0.3 mm. thick with rounded tips, were used to place lesions in cat brains. The lesions were created by employing the electrode as an anode and passing only direct current. Total charge (mC) was varied by either varying stimulus duration, keeping current
(ma.) constant, or by varying current (ma.), keeping duration constant. Both 1 mm. and 2 mm. tip exposures were tested. As was reported above, the greater the total charge (mC), whether increased by amperage or time, the larger the lesion. In the time dimension, greater variability in lesion size was evident as duration of stimulation was increased. Given the same total charge passed, however, the larger the tip (and hence the lower the charge density), the smaller the lesion.

Taking all this data into account, the critical factor believed to be operating in the creation of the lesion was the body's ability to handle the toxic products which resulted from the passage of electrical current. Concentrating these products in a small area, as was done by using the same current with a smaller tip, made the task more difficult. Lengthening the duration, even though total charge was constant, permitted, in some cases at least, removal of some of these products (perhaps where the lesion was created in an area of high metabolic activity such as near a blood vessel). Durations of less than 30 sec. within the parameter ranges used, produced discrete lesions. This study, in particular, underlines the importance of considering tissue variables when making lesions.

The progressive changes in lesion morphology that occur over time were ably pointed out by Wolf and DiCara (1969) as well as others (e.g., MacIntyre et al., 1959; Konovalova, 1968). Lesions were placed in rat brains with stainless steel insect pins, insulated except for 0.3 mm. at the tip. Constant current lesioning stimuli were administered for 6 sec. at 08., 1.2, or 1.6 ma. The animals were sacrificed and histology was performed 1 hr., 1 day, and 1, 2, 4, 8, and 16 weeks later. The apparent lesion size was found to increase as much as 400 percent from 1 hr. to 1 day and by the end of 16 weeks it could be as little as 20 percent of its maximal size. These authors detail the progressive changes in morphology which occur and suggest the possible underlying mechanisms. After the lesion has taken place, some cells around the perimeter are functionally dead but have been “fixed” by the current so they appear normal. Dead and dying tissue set up the irritative mechanisms which call forth the body's “healing mechanisms” (inflammation, edema, phagocytes, etc.). This peak lasts from 1 to 7 days. When the area has been cleaned up through time, surrounding tissue, probably as a result of mechanical pressure, begins invading the cavity formed by the removed tissue.

It is clear from these observations that great care must be taken in making parametric comparisons of lesion size. This is especially true in humans where there is no control over the interval between lesioning and histology.

It has been suggested (Wolf and DiCara, 1969) that there may be a difference in the reaction of tissue, in different locations in the brain (especially gray matter versus white matter), to coagulation currents, implying differences, perhaps in overall tissue resistance or sensitivity to
current. Wolf and DiCara (1969) indeed found different-sized lesions in the hypothalamus and caudate. Brudzyński (1971) found lesions only slightly larger in tracts and argued, however, that it is more likely that local metabolic differences rather than structural differences are the crucial factors, although even orientation of cells or fibers may play a role (i.e., tracts are in laminated channels).

When current is passed, both heat and toxic elements represent the adverse local conditions. Local blood and cerebrospinal fluid (CSF) flow can dissipate some of these effects, as can other metabolic mechanisms. In addition, current has been shown to flow along the surface of vessels resulting in an enlargement of the lesion. As long as these factors remain difficult to assess in lesion formation, there will be variability in the size and shape of lesions.

Radiofrequency Lesions

Radiofrequency (RF) lesions are also produced by the passage of electric current through electrodes, but the major difference lies in the fact that biphasic pulses are introduced at very high frequencies. The result is that the effects of electrolytic products on tissue are minimized and the lesion is produced by the heat generated at the tip. Since a relatively simple relationship exists between tip temperature and lesion size (Aronow, 1960), a tiny thermistor is often placed near the electrode tip to monitor the temperature. Often the electrodes are tested in egg white to see how large an area is coagulated (e.g., Fager, 1965).

The usual design for RF electrodes is similar to monopolar or concentric bipolar macroelectrodes used for stimulation of the brain. Stainless steel, insulated except for several millimeters at the tip, is often used. One variation worth noting is a stylet electrode described by Spiegel et al. (1965) and Spiegel and Wycis (1962) and modified by Szekely et al. (1965), as reproduced in Figure 16. The basic design is a hollow tube, closed at the end except for a small hole slightly to the side at the tip. An inner small-diameter (0.25 mm) stylet can be pushed through this hole so that it protrudes at an angle for about 2.5 mm. A thermistor in the tip monitors temperature. Although somewhat larger than many probes (2 mm. diameter), it is far more versatile in that a large amount of tissue is potentially accessible by lowering the probe to different depths and by turning it any amount in a 360 deg. circle. This is a distinct advantage since the best radiographic placement of electrodes in the human brain has a wide error factor and since repositioning an electrode within a small localized area represents an increased hazard to the patient. The stylet can be used in various positions at lower frequencies to test the function of the area until the correct location is found, then the lesion can be made in that location.
A major problem with the Spiegel et al. (1965) and Spiegel and Wycis (1962) design according to Szekely et al. (1965) is that a capacitance was set up between the active electrode and the brain tissue because of the outer sheath. The effect was a leakage of current which produced a lesion in the puncture canal. To remedy this an RF coil was placed parallel to the active electrode and the outer sheath. They reported that the situation improved in terms of reducing the variability of the size of the lesion. Nevertheless, evidence of small hemorrhages and coagulation around the puncture canal was still found, the average puncture canal lesion being 0.5 to 1.5 mm. wide. To keep hemorrhaging to a minimum they recommended slow insertion of the probe (to push aside large blood vessels).
There are certain variables which should be considered relative to radiofrequency lesions. One of the advantages of RF lesioning techniques is that at low values, as with cryoprobes, a “reversible lesion” is produced. That is, cooling a cryoprobe to 19 deg. C. will interfere with brain function in that area so that the effects of lesioning can be anticipated before the temperature is lowered still further to freeze and kill the tissue. In the same manner, passing current which heats an RF probe to somewhere between 40 deg. C. and 49 deg. C. can interfere with the function of that area enabling assessment of the future lesion (Brodkey et al., 1964). The RF probes have the additional advantage of being able to pass low frequency current to evoke normal behavior for that area; this was not possible in the cryoprobe (Fager, 1965).

Increasing the temperature to 75 deg. C. and maintaining it there for a period of time is sufficient to create a permanent lesion. The size of the lesion will depend on how high the temperature is and how long it is applied. To a certain extent, lesions can be enlarged by reheating the area, i.e., extending the total duration (Fager, 1965).

An interesting comparison was made by Mark et al. (1965) of the difference between heat-produced and cold-produced lesions, at least insofar as their effect on the cerebral cortex is concerned. The freezing lesions were produced by a nitrogen probe 2.2 mm. in diameter, cooled to -70 deg. C. to -190 deg. C., applied for 1 min. Heat lesions were performed by applying a 1.6-mm. RF probe and heating the tissue to 70 deg. C. to 90 deg. C. for 1 min. Lesions produced by freezing always caused wide-spread hemorrhaging which was fully developed within 15 min. In most cases the RF lesions were not noticeably free of bleeding. In cases where lesions were produced with temperatures less than 60 deg. C. to 80 deg. C., blood vessels were commonly spared. Using temperatures in excess of 100 deg. C. near major blood vessels can cause them to rupture. Inserting a scalpel blade into the center of these lesions further emphasized these differences—no bleeding was noted in the heat-lesioned area, while profuse and persistent bleeding occurred in the area that had been frozen.

Fox (1970) studied a number of the variables affecting lesion size when RF current is used in cordotomies. He varied electrode tip exposure, amperage, and duration of stimulation. In addition, two electrode types were used to apply the RF current (500,000 Hz): a monopolar stylet obtained from 22-gauge spinal needle (0.4 mm. diameter) insulated with vinyl tubing and a bipolar coaxial electrode. Tip exposure was 1, 2, 3, or 4 mm.; amperage was 25, 50, 75, or 100 ma.; duration was 10 or 60 sec.

The results were interpreted in terms of the events which occur at the electrode-tissue interface. Very simply, the amount of destruction depends on the local tissue temperature. Local tissue temperature, how-
ever, depends on two major factors—the buildup of energy at the electrode and the rate of heat dissipation in the tissue.

Energy buildup, or power, at the electrode tip is related to both voltage and amperage by the formula \( P = I \times V \). To determine the amount of heat in a given volume of tissue, power per unit of volume or power-density is the critical factor. The same energy spread over a smaller electrode tip results in greater heat per unit volume of tissue. Thus lesion size can be increased either by increasing the current or by decreasing the amount of exposed electrode tip.

In brain tissue, heat is conducted away from the heat source in such a manner that if a very low temperature were continuously applied, the tissue could dissipate the heat with no resultant damage to tissue. Radiofrequency stimulation is intended to heat up the local tissue faster than the heat can be dissipated, which results in the destruction of local tissue. However, when too great a temperature is reached too quickly, the tissue will “boil and fry” and the product of this reaction serves to insulate the electrode and prevent passage of current. This phenomenon was found to be more likely to occur with small tips, shorter durations, high voltages (i.e., when power density is high), as well as with bipolar electrodes. The net result is a smaller lesion which cannot be increased in size because of the inability to pass further current.

**RECORDING ELECTRODES**

**Brain Recording**

Man’s curiosity about how his own brain works has understandably led him to try to monitor its activity. It seems that if one could observe the activities in various regions of the brain as they correlate with each other and with overt behavior, and if one could track the spatial and temporal events, in abnormal as well as normal states, then one could go a long way toward understanding the brain. Two major problems face the determined scientist, however. First, as is the case with most measuring instruments, to record is to interfere. With the exception of surface EEG recordings whose information is limited, one of the trickiest problems has been to minimize the trauma associated with electrode implantation. The second major problem is the difficulty encountered in reproducing, with some degree of accuracy, the events which are taking place at the electrode tip. The electrical event is on the order of a fraction of a volt. Between this tiny entity and the display device chosen to represent it, lie many potential sources of distortion including the electrode-tissue interface, the electrode proper, electrode leads, and various amplifiers.

The sections that follow will outline the ways in which these problems have been tackled. In addition, brief mention will be given to the mea-
Measurement of nonneural events in the brain (oxygen availability, hydrogen gas measurements, and blood flow). While strictly outside the scope of measurement of brain activity, they do bear on some of the problems related to brain viability. Briefly, this discussion of the requirements for recording electrodes will cover both clinical considerations, including electrode materials, mechanical factors, sampling factors, and electrode designs, and electrical considerations.

When implanting recording electrodes, there are certain clinical considerations, one of which is the choice of electrode material. Any material which when passively implanted causes a tissue reaction is unsuitable for electrode purposes. Tissue reactions to common electrode and insulation materials have already been covered in the section on stimulating electrodes and will not be repeated here. However, the difference between stimulating and recording electrodes necessitates consideration of some other factors. First, as compared to prosthetic devices, the length of time the recording electrode stays in the body is much shorter. Second, the current which passes through the recording electrode is considerably less. Third, often it is not the metal itself which is in contact with the tissue, but rather some electro-deposited coating.

Recording from the brain may take place over a period of several hours (technically outside of the scope of this review) or up to several months. Most noble metals and stainless steel electrodes are satisfactory in all cases. However, these metals are sometimes unsuitable for mechanical, electrical, economical, or other reasons. It becomes necessary, then, to use a more toxic metal, if the recording period is less than the period necessary for the development of tissue reaction.

For example, Robinson and Johnson (1961) demonstrated that for implanted silver wires 125 μ in diameter, a violent tissue reaction occurred, but that it reached its peak (2 mm. to 3.75 mm. diameter zone of damage) in 7 days. Buser et al. (1972) employed silver ring electrodes to explore brain functioning in a 3-to-5-hour experiment, and not only recorded but also stimulated through the same type of electrode. It is presumed that in such a short period of time tissue reaction effects would not affect the results. (The authors reported no systematic changes which might indicate that tissue damage was affecting their results.) On the other hand, when a study is done (such as Buser's) where the tissue is known to be epileptic, it would perhaps be wiser to employ electrodes considered to be relatively inert to avoid any possible untoward effects.

Passage of stimulating current through many types of electrodes will corrode the tips, as was seen earlier in the stimulation sections. Such is not the case in recording electrodes where only minute voltages on the order of microvolts are involved. Here, the most serious source of corrosion is the extracellular fluid. It should be mentioned, however,
that with several of the techniques outlined below, small applied voltages (0.65 to 1.0 v.) are employed. Platinum, like gold, would be preferable in such cases, and one should also be aware of the electrolytic actions involved.

In some electrodes the exposed surface is coated with a material by electrodeposition (e.g., platinum black on a platinum-iridium electrode). The irregular surface that is produced results in a reduction in electrode impedance, which in turn improves the quality of the recording. Chlorided silver is known to be toxic in the brain (Fishcher et al., 1961); the potential toxicity of other surface platings should be examined before they are implanted in humans.

When an electrode is inserted into the brain for any purpose, the prime consideration should be that it do as little tissue damage as possible. It has already been pointed out in the section on stimulation that electrodes should be as small as possible and that they should not have any irregularities that can tear tissue and vessels on insertion. In addition, some people (e.g., Dymond et al., 1972) feel that the electrode must also be flexible enough to "give" with brain movements, to prevent it from slicing through tissue. These factors deserve reemphasis in light of the current trend toward using fine wire in multiples. Such use often involves twisting or cementing wires together which, if not closely scrutinized, can result in irregular configurations. Frequently, because the bundle of wires is by itself not stiff enough, a guiding device is required. Care should be taken that this device not cause trauma, especially if the device is to be removed once the wires are in place.

For large implant devices which may include some combination of electrodes, cannulas, and stylets where the total diameter is on the order of 1 mm., it is advisable to have a blunt rather than a sharp tip. Although a fairly large path of neural tissue will be destroyed by the electrode because of its diameter, blood vessels will be pushed aside rather than pierced. The latter event can create far more extensive damage than that caused by mechanical displacement of tissue. The frequent, successful use of this technique provides an argument for its safety.

In the case of fine wire implants, if individual strands are bundled together, they have the same potential to damage tissue as a larger-diameter single electrode. However, if each wire follows its own path, very little brain tissue damage occurs and penetrated blood vessels usually will seal themselves off.

Although any unnecessary damage to the brain should, for ethical reasons, be avoided in all cases, it is doubly important when the electrodes are for recording purposes because tissue damage can alter the events that are recorded. In the extreme case, the tissue reaction to injury (edema, encapsulation, necrosis, macrophage invasion) can prevent any recording from being obtained. But even slight damage can
alter the spontaneous activity of the tissue in that area and lead to erroneous conclusions about its behavior.

In order to understand the mass of heterogeneous tissue of the brain, especially in cases where pathological diagnosis is involved, it is desirable to sample as much tissue as possible, while keeping damage to a minimum. One way this can be done is simply to implant a number of electrodes in different sites in the brain. As an example, Crandall and colleagues (1963) routinely implanted bipolar macroelectrodes in three sites in the pes hippocampi and hippocampal gyrus on both sides (i.e., a total of six locations) for the diagnosis of psychomotor epilepsy. Each electrode was a standard concentric type. A variation of this technique which greatly increases the size of the sample is to substitute multiple-contact electrodes for the simple bipolar design. For instance, eight chronic depth electrodes, each consisting of six contacts were used by Nashold et al. (1972). These can be in the form of a bundle of wires, usually 8 to 10 per bundle, which are twisted and/or cemented together for structural support or are cemented on some rigid strut (Ray, 1968). The area of tissue sampled by each multiple electrode can further be increased by staggering the surfaces which have been exposed for recording so that they lie anywhere from 1 to 5 mm. apart along the length of the probe (Ray, 1968; Buser et al., 1972; Nashold et al., 1972). Of course, recording can be done between any two points on the probe and can involve a distance of several centimeters. In the case of fine wire electrodes, tips can be made to spray out from each other as well, to increase the sampling region (Babb et al., 1973). Finally, the sampling region can also be improved by using a movable drive to advance the electrode through a large body of tissue (e.g., Blum and Feldman, 1965; Marg and Adams, 1967).

Not only are multiple recordings important from the point of view of reliability, but also they can provide a great deal of information concerning the functional interrelationships of various brain sites. A study was conducted by Buser et al. (1972) which was specifically aimed at this purpose. Using cross-correlations of activity in various regions of the brain, they were able to outline various functional connections in both normal and epileptic tissue of the limbic system. It should also be noted that the power of these multiple-site techniques can be increased further by implanting in bilaterally symmetrical areas. This has been especially true in cases where localization of abnormal tissue is required prior to surgical removal or destruction of tissue.

In order to appreciate how the above factors have been incorporated into electrode designs, the following paragraphs will briefly review some representative examples and will consider the kinds of measurements that they were designed to obtain. Although one type of electrode system design tends to merge into the other, the electrode systems can be
divided into macroelectrodes (which sample relatively large fields of neurons) and microelectrodes (which sample individual cells).

Nashold and colleagues (1972) chronically implanted macroelectrodes made of bundles of wires bilaterally in symmetrical sites as part of a diagnostic procedure to determine the feasibility of corrective surgery for centrencephalic epilepsy. Of specific interest was the extent of subcortical involvement in this disease.

Each electrode was made up of six Teflon-coated stainless steel wires. Each wire was bared of insulation for 3 mm. (1 mm. in the midbrain), and arranged so that the intercontact distances, center to center, were 5 mm. apart. Within each suspected area, then, a fairly wide range of tissue, including cortical tissue, could be sampled. Furthermore, it was possible to stimulate between two points while recording from other contacts on the same or a distant electrode bundle. Thus, during a spontaneous or evoked seizure, the authors could examine the origin and spread of epileptic activity to determine if a single or multiple focus was involved.

Buser and coworkers (1972) were also interested in mutual relationships among various areas in the limbic system. Their techniques, however, employed very brief discrete electrical stimuli, and the multiple contact electrodes were used to pick up remote evoked activity, either on the same electrode or at more distant points including the opposite hemisphere.

Although not strictly a chronic implant (lasting 3 to 5 hours), the patient was awake throughout the procedure. From five to ten electrode arrays were introduced, each with 5 to 15 contacts. The leads, each consisting of a 2.45 mm. diameter silver ring, were spaced successively 1.5 mm. apart. Recording was bipolar (usually between two adjacent leads) and stimulation was also possible. By observing either simultaneous events in different regions during spontaneous seizure activity or responses to stimulations, it was possible to determine normal and abnormal connections among anatomical areas and to trace the development of seizure activity.

Ray (1966, 1968) presented two versions of a multipurpose brain electrode. In one, a central core of 24-gauge stainless steel tubing is surrounded by 18 fine wires. Through the central cannula microelectrode syringes for injection or probes for lesioning can be passed. The fine wires (diameter, 0.0035 in.) which circle the hollow tubing and are bonded to it with insulating material are made of a 90 percent platinum and 10 percent iridium alloy. The contact surface for each wire is obtained by simply scraping away 0.75 mm. × 1.00 mm. of insulation after manufacture and platinizing the exposed area. The spacing of these exposed surfaces can be close together or spread out over the length of the probe, depending on the area of sampling desired. In the
other version there is no central cannula. Instead, 37 wires are bonded together in a stepwise arrangement as shown in Figure 17, and again insulation is scraped away to form the contacts. Despite the great number of contacts, the whole array is only 0.75 mm. in diameter. The surface configuration is made smooth so that tissue will not invade such spaces as exist in a twisted wire probe. Since the exact location of the exposed contacts is known, the area from which recordings are made can be located accurately. However, once inserted, the probe cannot be adjusted.

The whole unit is placed in the skull through a guide screw and is held in a retaining cup by a retaining ring. During recording sessions, leads are plugged directly into the unit at the skin surface—there are no trailing leads with adaptor plug all wrapped up in bandages. The probe is stiff and plugging or unplugging the patient for recording places stress directly on the electrode itself. Should the unit loosen in the skull, damage to the brain could result. Nevertheless, the author reports few, if any, clinical complications in 2- to 4-week periods of implantation.

With or without the central hollow core, the multiple-contact probe can be a very versatile instrument. To date, Ray (1966, 1968) and Ray and Vogel (1972) have employed it for recording spontaneous electrical activity, evoking electrical activity by stimulation through the same or a
distant probe, measuring oxygen availability, detecting the presence of hydrogen, assessing the permeability of the blood-brain barrier, and for measuring the a.c. impedance of a region of brain tissue. The authors project future use of the probe for measuring pH, lactate, and glucose.

Oxygen availability can also be measured. When a noble metal is implanted in the brain, a nonpolarizable electrode is placed on the skin surface, and a voltage is applied between them (−0.65 v.), the current flow will vary with the amount of oxygen which is available near the depth electrode. Monitoring these current fluctuations, then, is a simple technique for measuring oxygen availability in the brain (Cooper, 1963).

Hydrogen clearance can be measured in a similar fashion (i.e., monitoring the current flow between a nonpolarizable surface electrode and a depth probe). Hydrogen molecules are adsorbed on the platinum surface, markedly altering the potential difference between the two electrodes (Ray, 1968). Similar curves were found for the detection of vitamin C in the region of a polarized depth electrode. Since ascorbic acid only passes the blood-brain barrier when it is not functioning properly and since this failure can occur under conditions of brain trauma, Ray (1968) suggested this as a possible technique to detect destructive lesions. Finally, Ray (1968) suggested that his electrode can be used as a medium for alternating current impedance methods. He pointed out that inasmuch as cellular metabolic changes can alter local impedance measurements, the technique can be used for identifying different anatomical areas, finding tumors, or detecting the responsiveness of certain brain areas to transient treatments administered to the subject.

Because the monitored behavior of a single cell conveys only a limited amount of information about the state of even a small region of brain tissue, it is highly desirable to sample as many neurons as possible. A variety of techniques using microelectrode systems have been developed to accomplish this end. Acute recording studies provide some innovations which can be adapted to chronic implantations and, therefore, will be considered first.

Jasper (1966) employed an electrode similar to the stylet electrode described in the section on lesioning, but employed it for recording, rather than stimulation, prior to lesioning. The recording electrode consisted of a tungsten wire stylet whose tip was sharpened to 1 to 2 μ. It was carried into the brain inside a 2-mm. diameter stainless steel shaft, then gradually advanced obliquely out an opening in the side of the shaft at the tip. Recordings could be made at any depth as the shaft penetrated the brain. The outlet hole could be turned in any direction in a full circle and the stylet could be advanced over a curved path for 10 mm. The potential sampling area, then, could be represented as a cylinder of brain tissue having a 6-mm. radius around the shaft and extending a
little below its tip. Using this device they were able to map the areas surrounding the shaft and thereby were able to decide on the extent and direction of the lesion. This technique has provided a means whereby the surgeon can compensate for anatomic variability and stereotaxic inaccuracies in the localization of tissue.

Verzeano et al. (1971) employed a system which, although not totally implantable, nevertheless did allow recordings in the awake subject. A screw guide (with stylet) was first implanted under general anesthesia. Several days later, with the patient awake, the stylet was removed and an 18-gauge stainless steel cannula inserted. Though the lumen of this, a single microelectrode was driven by means of a specially constructed microdrive, capable of advancing the electrode in steps of a fraction of a millimeter. The device was of such precision that the electrode would not make contact with the sides of the cannula. The electrode proper was a glass-coated platinum-iridium probe, which had been electrolytically sharpened. This device allowed the recording of single cells, groups of cells, and epileptiform waves, this providing a survey of the amount and distribution of activity in a neural target site traversed by the electrode. Such a survey is needed when examining a suspected epileptic focus.

Blum and Feldman (1965) presented a versatile device for moving four separate microelectrodes at one time. The device contained four internal shafts which could be moved and locked independently of each other. A small motor (powered by a 1½-v. battery) permitted advancement of the electrodes in controlled discrete steps, with 1-µ steps being ideal for contacting a neuron, and ¼-µ steps being used for coming closer to a neuron or for penetrating it. Faster speeds were available for traversing large areas of tissue to reach the target. The authors also presented a design for a combination micro-macroelectrode which could be used with this system (see Fig. 18). Basically, it has a concentric design, except that the central shaft is etched to a fine tip (1 to 2µ). The macroelectrode tip was formed by exposing a small amount of the tip of the 22-gauge stainless steel tubing forming the shaft of the electrode.

![Figure 18](image-url)
The microelectrodes in the preceding systems were rigid and required mounting devices which rendered them impractical for true chronic studies. An alternate approach, outlined in the following studies, is to employ flexible fine wires which can be used in chronic implantations.

In a 1967 paper by Marg and Adams, a small implantable microdrive, shown in Figure 19, was presented for use with bundles of fine wire microelectrodes. The guide for the shaft fits through a hole in, and is anchored to, the skull by screws. The device is manually powered and has the potential for a maximum descent of 3 mm. without turning the bundle (20 µ advance per turn). Marg and Adams also offered a method for locating the tips of the fine wire electrodes which involved passing a small current through the electrode (<1µa.) to form a small hydrogen bubble at the tip. The bubble was then localized by an echo-location device. Nevertheless, they reported that the accuracy of this technique is limited, with the error being on the order of 1 mm. or better (often the amount of separation between tips in a bundle of fine wires). Furthermore, gas evolution is deleterious to nearby tissue.

The fine wires used by Marg and Adams (1967) and Marg et al. (1970a) were 50 µ of straight tungsten wire, etched to a 1-µ tip and coated with Isonel 31 (15 coats). When these electrodes were implanted

![Figure 19](image-url)
as a wrapped bundle of five fine wires, they picked up very few neurons. A modified “free cluster” technique was subsequently employed which involved enclosing the tips of the bundle in a small piece of plastic tubing which was stopped by the brain surface as the wires were driven through it (i.e., it served as a guide for the wires). Recordings were much improved. It appears that damage is minimal with this microelectrode package. Although the tips are pointed, the wire is flexible enough so that if a blood vessel were encountered, the wire would bow or be deflected. The fact that the wires are not bound to each other enables this deflection to take place.

**FIGURE 20.**—Top: A microelectrode bundle with 8 microtips and a ground wire. Bottom: the plastic tube segment with a longitudinal slit and the suture thread. It guides the free cluster of microtips into the brain and may be completely removed immediately afterwards. (From Marg et al., 1970, by permission of S. Karger AG, Basel.)
In the later paper, this technique was modified slightly. The result is shown in Figure 20. Eight tungsten wires (same as before) plus a Teflon-coated stainless steel ground wire were soldered to an 8-prong amphenol connector. All but the distal 2 cm. were encased in PE-50 tubing. A small segment of PE-90 was slipped over the tips and served as a guide to prevent bowing of the wires as they penetrated the brain. A slit in this tubing allowed its removal once the electrodes were implanted. The tips were electrically bared for 1 mm. and were staggered, so the recording area was 2 to 4 mm.\(^3\).

Babb et al. (1973) also employed bundles of fine wires to record extracellular unit responses. Their system is shown schematically in Figure 21. Each wire was made from tungsten or an alloy of 79 percent platinum, 15 percent rhodium, and 6 percent ruthenium, and its diameter was 30 to 62.5 \(\mu\). The wire comes pre-insulated and the only tip care required is that they be cut blunt with a sharp pair of scissors. The wires were implanted in bundles of about seven, by being inserted through a \(\frac{1}{2}\)-mm.-diameter cannula of stainless steel tubing (which can also serve as a macroelectrode). The high elastic modulus of the wires gives them enough strength to be inserted. When all tips were flush with each other and together in a bundle they probably did as much damage as a macroelectrode and, furthermore, few cells were recorded. To increase

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the area sampled and to improve recording, the wires were prebent so that as they emerged through the end of the cannula (to extend 5 mm. beyond), each followed its own path. Damage to the delicate tips was prevented during insertion by a PE-10 tubing collar around the tips and a Delrin funnel around the top of the cannula. With such a system, spikes from single cells were clearly distinguishable from background activity.

The object of recording from the brain is to obtain some index of the electrochemical events which are taking place in the area, or areas, of interest to the experimenter. No device has been designed which accurately represents all dimensions of these events, but in most cases one or more features of the events can be enhanced in order to answer specific questions posed by the experimenter. For example, a vertical blip on an oscilloscope screen may not accurately trace the time course of ionic exchanges across a cell membrane, but it is sufficient to indicate that a nerve cell has fired. Since recording is done to obtain different sets of information, it is necessary to insure that the proper information is being recorded by investigating how different recording devices distort the electrochemical signals.

The simple act of placing an electrode wire in brain tissue (without passing current) is sufficient to generate a potential, which is referred to as a "half-cell" potential. The nature of this potential will depend on the composition of the electrode and electrolyte surrounding it. The latter will differ with extracellular and intracellular fluid and will also depend on local vascular supply or other factors in local chemistry. This potential can be many times larger than the signal to be measured and, therefore, can represent a serious source of distortion, especially with slow potentials. Furthermore, the potential sets up an ionic exchange between the electrode and the fluid, which could be mutually destructive. As has been noted earlier, tungsten, platinum and its alloys, gold, and stainless steel seem to be the best electrode materials, with silver and copper being particularly toxic.

In order to measure electrical events, two electrodes are necessary; therefore, all recordings are bipolar even though the electrodes may be dissimilar and placed at a great distance from each other as in "monopolar" recording. Traditional bipolar electrodes involve two contacts closely spaced together (usually ½ to 1 mm. apart in macroelectrodes). Since the activity recorded is the activity between the two electrodes, bipolar electrodes will more closely represent activity within a small localized region of the brain. In a monopolar arrangement, one electrode is usually placed in a target site, and the other on a distant neutral point with little activity of its own. The activity recorded, then, will be that which intervenes between the two contacts, but it can be attributed mostly to the events in the target areas. Although the sensitiv-
ty falls off rapidly as the distance of the electrode from the active tissue increases, monopolar recordings nevertheless will include a lot of irrelevant activity.

It two different metals are used for the two electrode contacts, a standing potential will exist which could distort the signal. Even two electrodes of the same material will not be identical (because of small deformities or oxidations, etc.) and small potentials can exist here too. Again, “nonpolarizable” electrodes can help overcome this effect.

The amount of bare wire exposed on the electrode will determine the amount of tissue from which it will record. Most macroelectrodes expose one to several square millimeters, while most extracellular microelectrodes have less than 100 \( \mu^2 \) exposed. Reducing the amount of tip exposure also raises the impedance of the electrode. (For example, standard bipolar or concentric electrodes might have an impedance of 5 to 15 Kohms in the EEG frequency range. Reducing the tip exposure to less than 100 \( \mu^2 \) might raise the impedance to 500 Kohms to 2 Mohms.) This increase in impedance occurs because, relative to a macroelectrode, the same voltage is being applied to a smaller area and the electrolytic processes can only proceed at a certain rate per exposed area. This high impedance poses further problems for amplification and display of the signal.

When small-tipped microelectrodes are used, a very special recording problem exists. In order to obtain high-fidelity recordings with such high-impedance electrodes, a high input impedance amplifier is necessary. That is, the amplifier is connected in series with the circuit which is measuring the voltage of the tissue. The total voltage drop in a series circuit consists of the voltage across the tissue and electrode, plus the voltage drop across the internal resistance of the amplifier. If the greater resistance is in the electrode, then most of the voltage drop occurs there, so there is little signal left to be amplified. A high-impedance input, however, guarantees that little voltage is lost in the tissue and electrode.

Discussion of the electrical requirements for recording and display systems which are appropriate to various types of biological signals lies outside the scope of this paper. The interested reader should consult Beddes (1972) or Frank and Becker (1964).

**Heart Recording**

Two kinds of heart recording will be considered here. The first type is conventional heart rate recording, a simple but valuable tool which serves as an all-purpose indicator of general body state (that is, heart rate changes can be used as indices of emotional states, physical exertion, disease, etc.). The other type deals with intracavitary diagnostic recordings which can include other indices besides the monitoring of muscular potentials.
The heart is a large and powerful muscle whose activity can be monitored over a wide part of the body. A standard clinical electrocardiogram (EKG) is obtained by placing surface electrodes, usually with paste electrolyte, on the right and left arms and left leg of a subject. He or she is required to lie still in a shielded chamber while recordings are made. A typical tracing of normal heart beat is represented in Figure 22 (the actual shape varies with electrode placement and other factors) for purposes of terminology. The P-wave is said to represent the spread of excitation over the atria; the QRS complex, the ventricular depolarization; and the T-wave, the ventricular repolarization. The QRS complex, or, to use its short form, the R-wave, is of large amplitude and generally survives a great deal of signal distortion. It is this element of the heart recording which is used for measuring heart rate.

Clinical diagnosis is one use for such recordings, but it is often desirable to monitor heart rate while a subject is performing any of a variety of tasks. Recently there has been a special interest in heart rate monitoring in the space program. Clearly, what is needed is a device which can be applied quickly (preferably without the use of paste, adhesives, complicated straps or other gimmicks) and can be worn for prolonged periods without tissue reaction or discomfort. Several designs have been tried by Richardson et al. (1968). One design involved intervention through the skin, and the others used surface electrodes attached by means of an elastic belt.

The subcutaneous electrode design utilized #5-0 braided stainless steel or #5-0 twisted tantalum sutures which were looped through the skin on the chest wall under local anesthetic and secured by spot-welding nickel alloy tape over the loose ends. All sharp edges were trimmed. Three sutures were used—one midway between the nipples, and the other two bilaterally below and slightly medial to the nipples. The ground lead was attached to the right suture. Removal was effected simply by clipping and slipping out the sutures. Some discomfort was evident with these electrodes; it peaked at 3 to 4 days after implantation. (Greater discomfort was observed with #2-0 sutures.) Although clipping

![Figure 22](image-url)
The edges and covering the sutures with tape reduces the possibility of heavy sutures interfering with clothing and other activities, the potential or interference is there. These electrodes proved unsatisfactory for clinical reasons. One-sixth of the implants became infected. Risk of infection may have been higher with the braided suture because of the greater number of spaces available for tissue invasion. On the other hand, this problem may have arisen because of variability in the depth of placement of the electrodes.

The surface electrodes were found to be superior for ease of application and trouble-free maintenance. Three variations were used, all attached to an elastic belt. In one, the orientation of electrodes was vertical, with the central electrode being common and being placed so that it lay 10 cm. to the left of the xyphoid over the cardiac apex. The other two lay slightly above and slightly below the common lead. A circumferential configuration was used for the other two belts tested. For these, the belt circled the body at the level of the bottom of the sternum. The common was located over the right midclavicular line; the other two leads were placed over the left midclavicular and left midcapular lines. In the 21 to 32 days that the belts were worn, the vertical configuration belt caused the most discomfort, but even in this case the discomfort was ignored after 2 to 3 days.

Two types of electrodes were used, either a lithium-chloride-impregnated piece of balsa wood or an anodized aluminum disc. Neither caused any chemical or mechanical skin reaction.

Several electrical considerations concerning heart rate recording should be mentioned. Suture electrodes had the best tissue contact, but, of the two, stainless steel appeared to be the most stable and had lower impedance properties (a mean of 9.12 Kohms compared to a mean of 2.8 Kohms for tantalum measured at 30 Hz with a 10µa. constant current source). However, the motion artifact appeared to be a serious problem.

Lithium chloride electrodes were made from smooth balsa wood blocks, 2.5 cm. x 1.25 cm. x 0.3 cm., impregnated with lithium chloride which served as the electrolytic interface material. The finished surface appeared dry and required no further treatment before it was applied to the skin. The resistance of the electrode itself was 15 Kohms. A special amplifier was required with high input impedance (1,000 Mohms) because of variability in impedance within and between electrodes. Tests, over the course of 3 or 4 weeks, showed no deterioration of signal (with a /N ratio of 3/1) over time, although electrode impedance was noted to increase steadily from 5 Kohms to 120 Kohms (hence the need for high input impedance). Although there were baseline shifts and increased incidence of noise during strong exercise, it never interfered with the ability of the cardio-tachometer to measure beats.
Typical potted insulated electrode. Middle: Electronic circuit for impedance match to permit use with conventional EKG equipment. Bottom: Insulated electrodes mounted on belt. (From Richardson et al., 1968.)
Insulated electrodes employed the principle of capacitive coupling to eliminate interface problems responsible for polarization and noise. The electrode unit, shown in Figure 23, consisted of an aluminum disc coated with aluminum oxide, which maintained the d.c. resistance at 30,000 Mohms, plus impedance-matching circuitry. All of this was housed inside a shield to protect it from stray electrical fields. In order to use the electrode with conventional EKG equipment, high impedance-matching circuitry was necessary. The biggest drawback in the system appeared to be the fact that motion artifacts could still be produced by variations in the capacity coupling.

**Intracardiac Recording**

It has been found that as an intracardiac electrode moves through various parts of the heart, slight changes occur in the electrocardiogram tracing thereby obtained (e.g., Hecht, 1946; Watson, 1964). These changes are reliable enough to serve as a kind of electronic “window” into the heart. The electrode is sensitive enough to enable the location of valves and also picks up a recognizable signal when the tip touches the endocardium. This has been especially useful in the placement of pacemaker electrodes.

There are several designs of intracardiac electrodes which can be used not only for monitoring the heart rate from directly within the heart, but which can also take other physiological measurements necessary for diagnosis of certain heart pathologies. These were presented in a paper by Rotem and Miller (1967). Three types were described, the first of which was a simple probe made of multistranded stainless steel wire (insulated with Teflon) having a 3-mm. platinum tip. This type was used for heart recording alone. The second, referred to as a “platinum electrode cardiac catheter,” had a single lumen through which substances could be introduced into the heart chambers. Several millimeters from the tip of the electrode was a platinum ring for recording. The third was designed especially for diagnosing valvular dysfunction. Two platinum contacts, spaced 10 cm. apart, were placed on a single catheter. Each had separate circuitry and separate reference electrodes.

In all three types of probes, the critical factor was the use of platinum tips. This enabled them to detect the presence of hydrogen of ascorbate in a manner which has been described in the section of this paper on brain recording.

The technique described by Rotem and Miller (1967) to detect septal defects (called “left-to-right shunts,” referring to the fact that blood flows unnaturally through a hole from one of the left chambers to one of the right) is summarized here. Taking a brief breath of hydrogen results in the gas passing very quickly into the blood stream and consequently into the left heart chambers via the pulmonary vein. In a normal heart its
return to the right chambers would be detected as a slowly rising “recirculation curve” which would appear some 5 to 9 sec. after inhalation. When a hole exists between the right and left chambers the hydrogen can be detected on the right side as a sudden deflection in baseline, beginning 1 to 4 sec. after inhalation. To locate the shunt, readings were begun in the pulmonary artery. The electrode was then retreated into the right ventricle and the hydrogen test repeated. The electrode was then repeatedly drawn back slightly and read again until a “recirculation curve” was obtained. The hole then was localized to the place of the last positive reading.

The principle involved in detecting valve dysfunction was similar, but the bipolar catheter was used. To study the integrity of the pulmonary valve, this catheter was introduced so the tip (with electrode) rested in the main pulmonary artery. The other electrode, then, lay in the right ventricle chamber. (Intracardiac EKGs confirmed correct placement of both electrodes.) Ascorbate was injected via the catheter. A slow “recirculation curve” was obtained at the right ventricle electrode when the valve was intact. Regurgitation resulting from a defective pulmonary valve produced a sudden deflection in response due to the backflow of ascorbate.

Before the development of this procedure, the only alternative was to take blood samples which tested for oxygen saturation in the various chambers to determine if “clean” blood from the lungs was leaking into the “dirty” venous blood of the right chambers. Such analysis was difficult, especially if the hole was small, and there was a time delay in obtaining results. In addition, the method was especially difficult in infants, where it was often needed. The disadvantages of cardiac catheterization itself have already been discussed and will not be repeated here.

The electrical technique used by Rotem and Miller (1967) involved a German silver electrode placed on the arm or leg as a reference point. A third lead (besides the inserted probe) grounded the patient. The leads were then run to the d.c. input of an EKG recorder which enabled the registering of both the baseline shift for hydrogen as well as the EKG. The authors’ caution regarding patient safety is worth repeating here. It is absolutely essential that the recording equipment be properly grounded and that other instruments and stray wires be kept away from the patient. This will avoid the possibility of shocking the patient or touching off an explosion of the hydrogen gas.

**Muscle Recording**

The work that has been done in recording from muscle falls into two major categories, studies of muscle contraction per se (by anatomists,
nesiologists, or clinicians diagnosing muscle disease, paresis, atrophy, etc.), and studies aimed at recording muscle contractions for the purpose of controlling prosthetic devices. Since the former studies involve shorter implantation times, while the latter concern more or less permanent devices, these research areas have diverged somewhat and, therefore, will be considered separately below. Nevertheless, it should be remembered that since the common goal is to record from muscle, these areas are not exclusive of each other.

**Temporary Muscle Recordings**

Electrodes have been implanted in a wide variety of skeletal muscles or as many different purposes, e.g., studies of isotonic and isometric contractions, fatigue, workings of speech muscles, latency of contraction over muscle surface. The type of electrode chosen depends on the needs of the experimenter. The types of electrodes which have been used to record from skeletal muscle fall into three main categories, surface, needle (monopolar and bipolar), and fine wire electrodes.

*Surface electrodes* usually consist of a metal disc (e.g., silver) which is applied to the skin over the muscle of interest. Contact can be improved by mechanical means such as straps, springs, or adhesives or by applying an electrolytic jelly to lower impedance at the tissue-electrode interface. Some investigators even recommend scraping the skin with fine sandpaper prior to applying the electrode.

Surface electrodes can be quickly applied, and are relatively safe — the major trauma occurs as a result of electrolyte irritation or mechanical rubbing if the subject is in motion. Indeed, it is these factors which limit the amount of time the electrodes can remain in place. However, if prolonged recordings are desired, Komi and Buskirk (1970) demonstrated that if the recording site was carefully marked with an indelible pot, recordings of muscle contractions taken at intervals of a matter of days were more reliable in terms of integrated gross EMG measures than were those obtained with repeatedly inserted fine wire electrodes. The unreliability of fine wires is probably due to the difficulty of reinserting the fine wires in exactly the same spot, and is probably also affected by local tissue trauma.

Horning and colleagues (1972) compared surface recordings with intramuscular coaxial and monopolar needle recordings when the measure of interest was the latency of evoked muscle responses in anterior tibial and abductor digiti minimi muscles. Surface recordings tended to have the shortest latency (nonsignificant), with good large amplitude deflections. Only the deepest-placed coaxial leads recorded comparable latencies; superficial intramuscular placements resulted in those that were much longer. These authors recommend the use of surface recordings for measures of latency of evoked muscle response,
except in cases where muscle is atrophic or where it lies deep to other muscle.

The major disadvantage with surface electrodes is that the recording is not made directly from the muscle, so potentials from irrelevant sources may interfere. The shape and meaning of the potentials picked up may be of some question. This is particularly true when the muscles are small and multiple, as is the case with laryngeal muscles. From a surface recording it is impossible to sort out individual muscle activity of the eight or so muscles involved.

For reasons of greater recording specificity, then, researchers have turned to the other two techniques: needle and fine wire recordings. Needle electrodes may be bipolar or monopolar (with remote skin reference). In comparing intramuscle coaxial and monopolar electrodes for evoked muscle response latencies, Horning and coworkers (1972) reported poorer quality recordings with monopolar leads.

The major disadvantages of needle electrodes, however, appear to relate to their size. First, they tend to move with muscular contractions which results in a distorted signal and may result in their coming out altogether. Second, they may interfere with the natural articulation of muscles. This would limit the conclusions which could be drawn from certain studies. Third, they induce enough discomfort on the part of the patient to further limit movements and also shorten the experimental time. Finally, there is danger of infection through the relatively large route through the skin. For these reasons, there has been a rise in the popularity of fine wire electrodes.

Fine wire microelectrodes in diameters on the order of 25 µ to 50 µ are usually constructed of “Karma” wire, an alloy of nickel, chromium, and aluminum insulated with polyurethane enamel. The insulation is removed to varying degrees and the tips bent to form a barb to prevent slippage. Insertion is via hypodermic needle (25 to 27 gauge) leaving the wires free to trail out through the skin to appropriate connectors. Removal is executed simply by pulling on the leads until they are freed.

Karma wire is the most popular and there has been no evidence of toxic tissue reaction due to the metal or insulation. Fine platinum wire has also been used (Steiner et al., 1972), as well as copper (Hirano, 1969). The latter might prove toxic if left in place for extended periods of time. Hirano (1969) usually studied laryngeal muscles over a period of only 20 to 30 min.

Fine wires are preferred for relatively long durations of implantation, because they are said to cause the patient little pain even when left in place for several days. Nevertheless, some patients do complain of discomfort and this should be given some consideration. The amount of pain, of course, may depend partly on the site of implantation, since innervation by pain fibers varies in different regions of the body.
Part of the pain is undoubtedly due to the hypodermic needles that are used as carriers for insertion. Jonsson and colleagues (1968) indeed demonstrated a positive correlation between the occurrence of bleeding on insertion or removal, and the presence of reported pain. Insertion trauma can be minimized by using needles which are small and sharp. Some of the pain, however, is specifically related to the fine wires themselves. It was shown by Jonsson et al. (1968) that at least in some cases inserting fine wires caused more pain than a control in which the carrier needle was inserted without wires, then removed. Furthermore, larger wire (0.5 mm. diameter) produced more pain than smaller (0.025 mm. diameter) wire. (It is worth noting that although the incidence of reports of discomfort was high in the Jonsson group's study, the subjects could have been influenced by the instructions and repeated questioning concerning pain.) Other factors such as depth of implant, angle of insertion, type of wire and movements involved could also be variables affecting the degree of pain or discomfort involved.

The chief arguments for using the fine wire electrodes are that by virtue of their size they produce little trauma, are very flexible, and can be comfortably tolerated for relatively long periods of time (up to several weeks). The same property which makes them advantageous, however, renders them very fragile. This presents problems for their manufacture and also results in a tendency for them to become displaced, fractured, or deformed in situ.

Jonsson and Reichmann (1969) demonstrated quite clearly with X-ray techniques and careful measurement the nature of displacement and deformation that occurs with fine wires (see Fig. 24). Barbed Karma wires were inserted into the flexor carpi ulnaris muscle. It was found that their greatest deformation occurred on the first contraction, when in the process more wire was usually drawn in. With successive relaxations and contractions of the muscle, wires were repeatedly kinked and stretched, sometimes pushing the wire back out the skin. The degree of deformation of the wire was related to its position of insertion along the extent of the muscle.

Migration of electrodes can be a serious problem if waveform or quantification of muscular contraction is desired. Indeed, the barbs are used in an attempt to prevent movement of the tips. Scott has suggested that the barbs will only prevent migration in one direction (personal communication in Jonsson and Bagge, 1968). Jonsson and Reichman (1969) found no evidence of migration deeper into muscle, although there were several cases of migration toward the point of insertion. In actual fact, though, the tips moved less than the rest of the wire; i.e., the deformed wire took on an arched configuration, and variability in tip location appeared to be on the order of only a few millimeters from locus of insertion (even though the length of drawn-in wire was on the order
of 7 to 17 mm.). It was believed that this deformation occurs because the inserted wire traverses several types of tissue on its way to target muscle. These layers of tissue will move differently relative to each other when the muscle contracts. Jonsson and Bagge (1968) reported more deformation with 0.025 mm. than with 0.05 mm. wire. In addition, the angle of insertion and action of the muscles affected the amount of wire pushed in or pulled out through the skin.

Another problem that arises in connection with lead migration is the change of the bipolar leads in relation to each other. Clearly, the character of the bipolar recording can be altered as tips move toward or away from each other and the recording can even be eliminated if they come in direct contact. "Barbing" the wires and cutting them to different
lengths can help but Scott and Thompson (1969) suggest that a better arrangement is to twist the leads together and strip off the insulation at different points (i.e., not both at the tips) as is shown in Figure 25. Even though the pair of leads may move, the exposed recording areas should remain in a constant relation to each other. The increased size of the implant may increase the trauma somewhat, but this would be offset by the increased strength.

![Figure 25](image)

Figure 25.—Sketch of twisted bipolar electrode in needle, showing controlled separation between bare areas. (From Scott and Thompson, 1969.)

There seems to be some controversy as to why, and sometimes whether, fine wire leads tend to fracture (see Jonsson and Bagge, 1968, p. 331, for arguments based on personal communications). Some of the reasons for breakage and suggested solutions will be considered here. There appear to be three main reasons why the leads might fracture: because of the handling and stripping of the insulation during manufacture; because of mechanical stress during insertion and removal; and because of mechanical stress due to muscular contractions.

Jonsson and Bagge (1968) found that in instances where leads fractured, 40 percent fractured at the bend in the wire, or at the junction between insulation and bared wire. Stress of insertion may account for some of these cases, but heating the wire during manufacture may also be to blame. A common method for removing insulation from the wire is to burn it off by match (e.g., Steiner et al., 1972), gas flame (Jonsson and Bagge, 1968), or hot soldering iron (Parker, 1968). It has been determined, however, that heating the wire will weaken it. Specifically, Steiner et al. (1972) compared the amount of weight that 25 µ platinum and Karma wire could support before and after flaring with a lighted match. The former supported 20 to 30 g before but only 10 g after heating before it would break. Karma wire supported 50 to 60 g before heating, 20 to 30 g after momentary heating, and only 10 to 20 g after long duration heating. While testing the force required to remove a single wire from a rat biceps femoris, they found it sometimes exceeded 10 g. Therefore it appears that heating the wire weakens it to such an extent that it is within range of its breaking point.

For these reasons and also because burning may leave an ash residue, Komi and Buskirk (1970) and Scott and Thompson (1969) have prefer-
red to use chemical strippers to remove insulation. (The former used semiliquid number 990 Insulation Stripper, Fidelity Chemical Products Corp.; the latter employed a solution containing formic acid, phenol, and ethylene glycol.) Such a procedure has the added advantage of permitting more control over the exact amount of insulation removed. It was especially useful for Scott and Thompson (1969), who exposed an area which was not at the electrode tip. More uniform electrodes mean more comparable recordings.

An alternative solution to the weakening and ash problems is simply to cut the wires blunt, removing no insulation. This has been the preferred technique of Hirano and Ohala (1969) and Parker (1968). Although this may introduce a recording problem because of higher electrode impedance, the problem of shorting of leads is nevertheless greatly reduced. This also makes greater localization within the recording area possible.

Damage to the leads because of handling during manufacture will always remain a problem, though to some extent precautions can reduce this damage. Steiner et al. (1972), for instance, have developed a clever jig for the manufacture of a six-contact electrode (see Fig. 26). It not only minimizes handling, but also standardizes the length (and spatial arrangement) of the tips. Jonsson and Bagge (1968) also found that 0.05-mm. diameter (50 µ) Karma wire is less likely to fracture than 0.025-mm. diameter wire. Since fractures tend to occur at the bend in the wire, some people prefer not to barb the wires. This might increase the electrode’s tendency to migrate, however. In addition to these precautions, one of the first preventatives is careful inspection and selection of wires before insertion.

The most common method of insertion is via a hypodermic syringe needle. Wires are inserted (2 to 6 wires, twisted or not) through the needle and bent back over the tip to form a barb. As the needle and electrodes are inserted, the bent angle and bared portions (if stripped) are subjected to a good deal of stress. It has been argued above that these regions have probably already been weakened by the manufacturing process. And, indeed, these are commonly found to be fracture points. Parker (1968) partly avoids this by inserting the tip through the needle, allowing the remainder of the wire to trail out on the exterior of the needle. Nevertheless, the angle portion still bears considerable stress on insertion.

Withdrawal of the insertion needle may also be a source of stress. Jonsson and Bagge (1968) for instance, observed the electrode would sometimes be pulled out for distances of up to 7 mm. as the insertion needle was removed. It is therefore important to be sure the leads can move freely in the needle before insertion. Parker (1968) has found that holding the wire with the finger while withdrawing the needle will also help prevent the fine wire from coming out.
The greatest stress probably occurs when the electrodes are removed, however, since they are simply pulled out against the resistance of the arbor. Jonsson and Bagge (1968) recommend removal with forceps whose tips are padded, by pulling slowly, 1 cm. at a time. Even this technique, however, produced fractures.

Jonsson and Bagge (1968) also reported in one experiment that 60 percent of the cases of fracture occurred neither at the bend in the wire nor in the uninsulated portion. Furthermore, wires simply inserted, when removed, never showed fracture. They therefore concluded that in he cases of fracture the wires probably broke because of the kinking which occurs with muscular contraction. Using the larger diameter (50 µ or 0.05 in.) wire reduces the possibility of fracture considerably and, presumably, leaving the implant in place for less time (i.e., fewer contractions) would also be of help.

Finally, Jonsson and Bagge (1968) reported no more pain associated with pieces of broken wire left in the muscle than that associated with successful needle deplantation, and they reported all signs of pain gone follow-ups of up to 1 month. Nevertheless, the fact that some frag-
ments as long as 43 cm. remained in muscle makes it desirable to develop techniques to eliminate electrode fracture. The long-range effect of these remaining fragments is unknown.

Many of the electrical considerations discussed in brain recording apply to muscle recording as well. Some of the factors unique to muscle recording will be covered briefly below.

Striate muscle cells are elongated segments of contractile tissue varying in length from 1 to 50 mm. or so and in diameter from 0.01 to 0.1 mm. These cells are organized into bundles which lie in parallel along the longitudinal extent of the limbs. Individual muscle cells are held together to form muscle segments by connective tissue (perimysium) and groups of muscle segments are surrounded by epimysium to form the whole muscle.

Innervation of muscle cells is not on a one-nerve-to-one-cell basis. Rather, one motoneuron in a bundle coming from the spinal cord will branch many times when it reaches the muscle with each axon branch innervating a separate muscle cell. The number of individual muscle cells excited by a single motor nerve may run as low as 3 (eye muscle) or as high as 150 or more (thigh muscle). Thus, when a single motor neuron fires, there may be, for instance, 50 individual muscle cells that contract in unison. This single motor neuron and all the muscle cells it innervates are called the motor unit.

The point of contact between the axon branch and the muscle cell is called the myoneural junction. An impulse from the axon arriving at this junction depolarizes the underlying tissue which, if it reaches a certain threshold, results in the initiation of a muscle action potential, a wave of depolarization which passes over the entire muscle cell in much the same manner as nerve depolarization. This, in turn, activates the contractile mechanism housed within the muscle.

From these considerations, it should be clear that even the firing of a single motor unit involves a variety of electrochemical events scattered over some distance. It should be equally clear that the recording of electrical events will depend on both the size and the placement of the electrodes, as well as other characteristics of the recording equipment.

Recordings from muscle are usually classified as gross or microelectrode recordings. However, there is actually a continuum of events which are recorded and which depend on the relative size and placement of each type of electrode. So-called "gross recordings" are usually employed when one is interested in recording the magnitude or pattern of muscular contractions. Recording with surface discs which have a large exposed surface will pick up motor units over a wide area, especially if monopolar recordings were used. Greater specificity can be obtained by placing two leads close together over the muscle. Horning and coworkers (1972) were able to obtain differences in average evoked
response latency as surface electrodes were placed 5, 9, or 15 cm. apart over the anterior tibial muscle.

Fine wire or needle electrodes with several square millimeters of exposed surface can record average activity over a more localized region such as one muscle in a group of closely packed muscles, or one muscle segment of many, especially if two leads are placed fairly close to one another (Guld et al., 1970). Because of this specificity, and because of the peculiar innervation of muscle, it should be noted that changing the position of one or more of these electrodes can alter the character of the signal. Shifting of needle electrodes and migration of fine wires have already been mentioned as problems with moving muscles. This makes it difficult to compare signals from time to time and from experiment to experiment (see Komi and Buskirk, 1970). The six contact electrode used by Steiner et al. (1972) may offer some remedy, since they claim that the contacts do not move and that the tips remain a constant distance from each other.

Fine wires or insulated needle electrodes with exposed surfaces of less than 1 mm.² are capable of monitoring the activity of single muscle cells or small groups of cells (Guld et al., 1970). They are especially useful for diagnosis of muscle diseases because they can pick up individual fibers and motor units which are not functioning normally. To allow this degree of specificity, bipolar leads should be implanted. This use was demonstrated by Hirano and Ohala (1969) with electrodes placed in the laryngeal muscles. Patterns of activity in two closely spaced muscles could be distinguished from one another and spikes from individual cells were clearly visible. One caution noted in this study with respect to small muscles is worthy of comment. When fine wires are inserted with syringe needles, the recording tips may be as much as 2 to 4 mm. from the syringe needle tip. This must be taken into account to insure that not only will the recording tips be deeply imbedded in muscle, but also that

FIGURE 27.—A, B. Possible faulty insertions of hooked-wire electrodes. C. Correct method of insertion. (From Hirano and Ohala, 1969.)
they will be in the correct muscle. To insure this where small, closely packed muscles are involved, they recommended insertion in the muscle at as sharp an angle as is practical (see Fig. 27).

The signal from gross records resembles noise and for this reason care should be taken that contact is good and that leads are not broken and cannot move so that the tips might touch. Otherwise, movement of the electrode will be misinterpreted as muscular activity. The problems of electrode movement and suggested solutions were discussed earlier. Because the signal resembles noise it is difficult to observe and quantify. Typically, then, the signal is rectified (usually with a diode) so the signal has one polarity sign; then it is integrated. Carrying the signal from the tissue to the amplifiers and ultimately to display devices will not be considered here. The interested reader is referred to a paper by Guld et al. (1970) which thoroughly deals with EMG instrumentation.

Long-Term Muscle Recordings (Prosthetic Devices)

A paper by Herberts (1969) presents an extensive history of work in limb prostheses and a detailed description of the factors that must be considered regarding both the patient and the prosthetic device. The main points relevant to this paper will be considered below but only references related to electrodes proper will be cited. The interested reader is referred to the original paper for more information.

In the past, prosthetic devices for limb amputees have required gross bodily movements to articulate a series of cables and harnesses in order to produce relatively simple movements. This was usually uncomfortable and fatiguing, and the net effect could not approach natural movement. In an attempt to improve the amputee's lot, a search has been undertaken to find a prosthetic (for amputees) or orthotic (for impaired muscle) device which has an external power source and provides a wide range of movements but which the amputee signals with his own remaining or deteriorated muscles. Specifically the aims have been to use myoelectric signals to initiate and control a variety of coordinated movements (such as rotating the hand or grasping an object); to incorporate feedback which is more natural and permits adjustment to variable loads; and to find electrodes that are nontoxic, nonirritable, durable, and capable of reproducing the required signal accurately despite fatigue and random variations in contraction.

The task at hand is to find enough active sites in the amputated or paralyzed limbs to provide signals, each of which will control a separate function (such as gripping, supination, pronation). It is also desirable that at each site the signal can be varied in such a manner as to produce graded control of each movement.

The sites available will depend on the location of the amputation (the
more proximal to the body, the fewer the muscles available); the extent of the injury (some muscles might be damaged above the stump); the procedures of surgery (the number of muscles left intact or functioning); and, in the case of paralysis, the number of muscles with some degree of function. Given that a signal is available at a site, its usefulness will depend further on the clarity and reliability of its recorded parameters (duration, amplitude, configuration) which in turn are dependent on whether the damage is neurogenic or myogenic in origin.

Ironically, the people who need prostheses or orthoses most are those with the fewest available sites. However, it is possible to use other sites or a different dimension of the signal to activate the device. Examples of other sites include unaffected muscles above the amputation site (such as biceps and triceps brachii in a below-elbow amputation), and normally "unused" muscles, such as the auricular muscles. (Surgeons should operate with preserving muscles for prostheses in mind.) If only one site is available, different frequencies or amplitudes might be used to trigger different functions. Even separate motor units in one muscle can be used. Such techniques place great demands on the accuracy of recording and amplifying equipment. More versatility can be incorporated if each signal, or signal dimension, is used to trigger a preprogrammed sequence of movements. Caution should be taken in such cases to prevent requiring too much attention on the part of the patient; otherwise, the effectiveness of the device is greatly reduced.

The basic element to be recorded is the motor unit. Under certain conditions it may be recorded alone, but usually it is picked up in multiples. When a single motor unit fires, a characteristic wave of electrical activity having a duration of about 7 to 10 msec. is recorded which is referred to as the motor unit action potential. It represents the summed activity of all the separate firings of the individual muscle cells in the motor unit; therefore, the duration, amplitude, and shape of this action potential are dictated by the number and spatial distribution of the muscle cells in the motor unit (and of course by the electrode type and location of placement). During weak contraction a single motor unit will fire at around 5 to 10/sec.; in strong contraction at about 20 to 50/sec.

When several motor units fire, as is the case in normal contraction, the picture gets more complicated. At weak contractions, individual motor units will be firing slowly, so relatively low frequencies will be evident. As tension increases the gross muscle signal begins to resemble noise; however, after the muscle has been contracting maximally for a while, fatigue sets in, which is characterized by low rates of firing (the muscle "shakes").

The above discussion refers to normally functioning muscle. Before these dimensions of muscular recording can be employed to operate prosthetic devices it is necessary to examine the changes that can occur in
muscle activity as a result of pathology. Damage to motor nerves reduces the total number of motor units firing although a totally denervated relaxed muscle shows random firing of individual muscle cells (fibrillar action potentials). Regenerating nerve fibers often contact other muscle cells, which can result in increasing the amplitude and duration of motor unit action potentials. On the other hand, disease of muscle usually affects muscle cells randomly, so while the total motor units may remain the same, individual action potentials may be of shorter duration and lower amplitude and may be polyphasic in form.

What are the parameters of a pathological muscle signal, then, which will make possible a number of different prosthetic movements and which will also allow proportional control for each? In addition to satisfying these requirements the signal characteristics must be reliable and must not be influenced by transient conditions such as fatigue.

Amplitude of contraction would appear to be a good choice for controlling a graded response, for even in a stump muscle amplitude of the signal tends to vary directly with strength of contraction. A different stump muscle could then be used for each different act to be performed by the prosthetic device. When too few muscles are available, however, different levels of amplitude could be used to control separate functions.

It is also possible to use the power spectrum (i.e., a frequency analysis) of the muscle signal. For instance, it is known that the spectrum is different for different muscles and shows characteristic changes with various levels of contraction. Since power spectra for damaged muscle would differ from normal spectra, separate profiles would have to be obtained from each recording site. The subject could then be trained to alter the frequency distribution in order to operate the prosthetic device. Finally, in some cases of severe trauma, it has been found that only one motor unit is functional in the remaining muscle. Even this can be trained to operate a simple-function prosthesis. Special considerations which limit the use of these parameters are discussed in more detail in Herberts (1969).

Needle electrodes and implanted wires running to the surface are undesirable for reasons of infection and/or discomfort to the patient. The only two practical alternatives are surface electrodes and totally implanted sensing devices. Dry surface electrodes are the least traumatic, but entail serious signal distortion. Surface electrodes which use electrolytic paste risk the danger of skin irritation with prolonged use.

Totally implantable electrodes would seem to be the ideal. A version by Hirsch et al. (1966) which was encased in epoxy has already been tested and found to cause little tissue reaction (except for the usual encapsulation). The chief problem seems to be the unreliability of contact with the muscle. A new vitreous carbon button electrode introduced by Kadefors et al. (1970) may represent a good compromise between
surface and totally implantable electrodes. This electrode was slightly smaller than conventional prosthetic surface electrodes (overall dimensions $5 \times 4$ mm.), formed in the shape of a spool or bobbin. It was implanted over the desired muscle area (under local anesthetic) so that only the surface “button” showed above the skin (see Fig. 28). The wound healed in 1 week and by 1 month the entire unit had stabilized. Skin tissue slowly grew under the electrode surface. Histology showed little inflammation and only a 1 to 2 mm. thick layer of connective tissue encapsulated the electrode. To a certain extent the electrode was pushed out about halfway but total rejection only occurred in one patient after bumping the electrode (5 months after implantation). The rejection took 2 days. Subjects reported no pain associated with the buttons unless bumped. They used their arms normally and forgot about the presence of the electrodes. This device may, however, be impractical in certain cases of amputation where the remaining stump skin is too thin or the tissue too sensitive to pain.

![Figure 28](image)

**Figure 28.**—The electrodes immediately after insertion. (From Kadefors et al., 1970.)

In order to use a signal to control a prosthetic device or orthotic device, the electrode first of all has to be capable of picking up the required information with as little distortion as possible. Electrode types will be considered here according to how they will distort the three parameters designated earlier as useful — amplitude, frequency, and single motor unit activity.
Dry surface electrodes, i.e., metal plates placed in direct contact with the skin, have very poor surface contact which results in a very high impedance. As a result, the amplitude of the signal is lowered and low frequencies are lost. Furthermore, a large movement artifact increases the noise level, which can be misinterpreted as signal.

The use of electrolytic paste with such electrodes will virtually eliminate the capacitance and reduce the noise artifact due to friction; however, prolonged use of such a paste has been found to irritate the skin. (Scraping of the skin with sandpaper to improve contact would likewise prove irritating.) These factors are especially important in amputees because often the skin of a stump is thin, scarred, or atrophic. Furthermore, some amputees have no sensation in the stump so damage can occur without their being aware of it. Finally, surface electrodes typically are large and make contact not with muscle, but with overlying skin. They therefore pick up potentials over a wide area, which also depends on how far apart they are spaced. The signal will be distorted as it passes through skin, fat, etc., and potentials other than muscle potentials will be picked up. These are serious problems if separate muscle signals are to be picked up to control different prosthetic functions.

Needle electrodes are not practical for long-term use because of discomfort and danger of infection.

Fine wire electrodes were reviewed earlier in some detail. These thin percutaneous electrodes have good contact with muscle, resolve single units well, and with proper amplification can be used for transmitting information regarding amplitude and frequency spectrum. Their range of pickup is small, however, which is a problem in pathological tissue where few units are available. The major drawbacks with this type are its tendency to fracture with prolonged use and the risk of infection along its percutaneous route.

Clearly what must be developed are totally implantable electrodes that can be placed in direct contact with muscle. Such placement will avoid most clinical problems and will also produce a signal with broader frequency range and better signal-to-noise ratio. Amplifying and transmitting circuitry can also be implanted with power induced from an external source. Such an electrode has already been implanted and tested by Hirsch et al. (1966). The Hirsch et al. (1966) device, shown in Figure 29, was encased in epoxy with gold wires contacting the muscle. Over time the device became encapsulated but this did not seriously affect the signal which was reliable and of high quality for at least a year. Although some cracks did develop in the epoxy, the weakest part of the electrode was the gold contact wires. This problem might be overcome by substituting better wires (such as Karma wire), or the whole unit might be changed to a capacitive electrode.
The vitreous carbon button electrode used by Kadefors et al. (1970) performed as well as a Beckman surface electrode applied to the same spot prior to surgery. The signal appeared remarkably stable over a 10-week period even though there clearly was growth of tissue underneath the electrode. The main advantage of the button electrode was a much lower impedance than the surface electrodes. This was likely due to the improved contact with the tissue. One disadvantage of the button electrode was that the material was so smooth that contact with external hardware was difficult. Materials electroplated to its surface merely peeled off. A gold-plated spring which was pressed over the button was needed to test the device.

**Digestive Tract Recordings**

Recording from the digestive tract (esophagus, stomach, small and large intestines, colon) in humans is still in its early stages. The data are sparse and techniques have not commanded the same attention as those for brain or skeletal muscle recording. The use of such techniques in the diagnosis of digestive maladies is to a large extent still unexplored, for the major reason that the recording of normal electrical activity is neither well documented nor well understood. Some of the reasons for lack of development within this area are the limited knowledge of smooth muscle activity, the inaccessibility of the tissue, and the question of contact even if the tissue can be reached.

Kohatsu (1970) has gathered together most of the current work relevant to human gastrography. (Only certain references will be cited here; the interested reader is referred to the original article for more information.)

In the human stomach, spontaneous rhythmic slow waves occur with a periodicity of 2.5 to 3.4 cycles per min. Animal experiments indicate that these waves appear whether or not a contraction occurs, and are propa-
gated throughout the proximal to distal pyloric length of the stomach at a rate, in humans, of approximately 5 to 7 mm./sec. These waves are myogenic in origin, apparently representing a low-amplitude (15 to 50 mv.) depolarization wave. Presumably there is a pacemaker, although it has not yet been unambiguously identified. Spikes waves occur only in association with contractions (possibly causing it) and are not propagated.

Three main types of recording from the stomach have been employed—implanted intragastric electrodes, swallowed intragastric tubes, and surface (skin) electrode recordings. Stainless steel electrodes implanted in humans (Kohatsu, 1970; Nelsen and Kohatsu, 1968) produce the clearest signals of both slow waves and spikes, but the technique entails all the hazards of surgical intervention. Recordings with skin surface Ag/AgCl electrodes produced just as good frequency representation of slow waves as with implanted electrodes. Since it is still not certain what dimensions of the gastric signal are important in diagnosing gastric dysfunction (i.e., amplitude, shape, or frequency of slow waves or spikes), it does not yet seem justified to employ surgical techniques until its diagnostic superiority has been proved. On the other hand, there does appear to be evidence that frequency analysis can be useful in diagnosing some illnesses.

As a compromise between surface and implanted procedures, attempts have been made to record signals from the stomach via swallowed electrodes. Earlier techniques employed silver discs (Colcher et al., 1959), silver chloride wicks (Colcher et al., 1959; Martin and Morton, 1952), and platinum balls (Fukushima et al., 1951) attached to balloons or tube carriers. Two main problems exist with such devices: an object is present in the stomach which may alter its resting activity, and the electrode-tissue contact is poor. Any movement at this interface would undoubtedly alter amplitude, wave shape, and spike measurements. More recently, a suction electrode has been used by Oi et al. (1967), Shiratori et al. (1967, 1969), and Oi and Tanaka (1965). This electrode consists of a nasogastric tube with needles or stainless steel bars located near the tip. Electrode-tissue contact is obtained by applying suction at the open tip. The result has been high-quality recording; however, suction can be maintained only for relatively short periods of time. If long-term recording of natural gastric activity is desired, cutaneous electrodes may be the best technique, at least for frequency analysis.

As with gastric recordings, slow-wave activity and superimposed spikes have also been recorded from the small intestine (e.g., Christensen et al., 1964) and from parts of the colon (Provenzale and Pisano, 1971). Slow waves 9 to 16 cycles per min. (140 μv.; 4-sec. duration) with numerous superimposed bursts of 150 μv. spikes were commonly found in transverse and descending colon. Although slow waves were in evi-
dence in the ascending and sigmoid colons, they did not show the rhythmic regularity seen in the other areas. The sigmoid colon showed bursts of spikes; the ascending showed very few.

Two types of electrodes were used in the Provenzale and Pisano (1971) study, extraluminal electrodes placed during abdominal surgery, and intraluminal electrodes which were inserted transanally. The extraluminal types were wick or glass pore electrodes applied only during surgery or were spiral nonpolarizable electrodes on polyethylene plates (see Fig. 30) left in place for 2 to 3 weeks after surgery.

The intraluminal electrodes were more difficult to insert than one might anticipate. Although the colon appears to be easily accessible, the most direct route involves forcing an electrode against the natural flow. A clever, though seemingly uncomfortable, technique was developed to insert a pulley system via the oral-aboral route. Once in place the electrodes could easily be pulled into the colon by working from the anal end (see the paper for details). The electrode proper, shown in Figure 30, consisted of bipolar contacts spaced 1 to 2 mm. apart which were encased in a Plexiglas cup. Contact with the colon mucosa was maintained by suction. Although the authors reported that similar recordings were obtained with extra- and intraluminal electrodes, they do admit that contact with the suction electrodes was not very good. Movement artifacts were obtained during respiration and coughing, and on occasions.

![Diagram showing two types of electrodes used to record electrical activity of human colon in vivo. Extraluminal serous electrodes (right) and intraluminal mucous suction electrodes (left). (From Provenzale and Pisano, 1971.)](image-url)
the electrode itself moved. It is not surprising that suction was sometimes ineffective in maintaining contact in light of the large size of the Plexiglas cup (7 mm. diameter × 5 mm. depth).

Edmonds and Cronquist (1970) have developed a millivoltmeter and electrodes specially adapted for measurement of the electrical potential difference (usually less than 100 mv.) across the mucosal epithelium of the distal colon and rectum. Changes in this potential have been found to serve as indices of aldosteronism in hypertension patients.

The rectal probe used is shown in Figure 31 along with the reference electrode to be placed on the skin of the forearm. Both consisted of Ag/AgCl leads housed in Perspex (Plexiglas) cases with plugs of NaCl 150 mm. Agar 3 percent forming the electrolytic medium between electrode and recording surface. The shape of the rectal probe was designed so that it could be inserted without endoscopy, and so that it would do no tissue damage.

To effect recording, the skin was cleansed with alcohol, then NaCl 150 mm. before the reference electrode was strapped to the forearm. A reading was taken on the skin just outside the anus, then the probe was inserted about 8 cm. and a second reading taken. The mucosal potential minus the skin potential determined the rectal potential.

Because of the high resistance of the tissue and the saline bridge, normally a high input impedance to the voltmeter would be required. However, the authors used an FET input stage with high input impedance but lower output impedance, which is suitable for the input of

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**Figure 31.**—a. Reference electrode (1 cm. × 2 cm. dia.); b. Probe electrode (10 cm. × 0.5 cm. dia.). (From Edmonds and Cronquist, 1970.)
conventional transistors. The output of these transistors was low enough to allow the use of a battery-powered millivoltmeter, so an electronic voltmeter was not required. The whole unit is small, light, and easy to use. A circuit diagram was presented in the paper.

Recordings from the Spinal Cord

Brindley (1972) reported a device which has thus far been used only in animals for long-term recording of spinal root nerves. The device, shown in Figure 32, consists of three separate clusters of four channels — the channels spaced about ½ mm. apart, each cluster about 10 mm. apart. A separate spinal root was inserted into each channel (under special conditions a spinal root could also be split longitudinally and the separate parts placed in separate channels) and sealed closed (under a microscope) with a small amount of medical adhesive. The body of the implant was made of silicone rubber (Silesol SR 600 and Dow Corning Medical Adhesive Type A), the contacts of platinum wire. The author reported recording from 12 different dorsal or spinal roots in the baboon, but estimated that recordings from 20 are possible. Electrodes have been in place for 20 months with no distinctive threshold or muscle alterations. As reported, the technique is not suitable for humans since it involves removal of part of several vertebrae.
Recordings from the spinal cord of man have been limited until recently by the lack of appropriate placing devices. In the past, techniques were limited to using the conventional stereotaxic instrument (Rand et al., 1965), X-rays (Gildenberg et al., 1967), or direct visualization (Puletti and Blomquist, 1967). To remedy this, Hitchcock (1969) developed a special stereotaxic device for percutaneous spinal cord electrode placements.

Hitchcock and Lewin (1969) demonstrated the usefulness of this device. Concentric electrodes were implanted aimed at the cuneate fasciculus, gracile fasciculus, spinal trigeminal nucleus, and spinothalamic tracts. The electrode consisted of insulated 22-gauge stainless steel tubing. In its central lumen was a gold wire insulated except for 1 mm. at the tip. Electrical activity in these sites was evoked by appropriate body movements or tactile stimuli. Recordings clearly showed increased amplitude and frequency with these manipulations. It is hoped that this technique will pave the way for further exploration of the anatomy and physiology of the human spinal cord.

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