CLINICAL PROGRESS

External and Internal Electric Cardiac Pacemakers

By Paul M. Zoll, M.D., and Arthur J. Linenthal, M.D.

It has long been known that electric currents have important effects on the heart as they do on other excitable tissues. Only recently, however, have techniques been developed for the therapeutic use of electric currents on the human heart. Two important clinical applications have now been established: electric stimulation of the heart for the production of an effective beat, which is the subject of this review, and electric countershock for the termination of ventricular fibrillation and other serious tachycardias.

Direct electric stimulation of the heart is a familiar laboratory technic. It is commonly demonstrated in elementary courses in physiology, it provides control of the heart rate in many physiologic and pharmacologic experiments, and much of our knowledge of cardiac excitability has developed from it. The clinical use of direct electric cardiac stimulation via a percutaneous needle electrode in the atrium for resuscitation from cardiac arrest was suggested by Hyman in 1932. Electric stimulation of the heart was first applied successfully in man in 1952 externally by way of electrodes on the chest wall.

External Cardiac Stimulation

Indications

External electric stimulation of the heart is now widely used for the emergency resuscitation of patients from ventricular standstill of any etiology (fig. 1). Its successful use has been reported in Stokes-Adams disease, in acute myocardial infarction, in reflex vagal standstill, in standstill due to cardiac drugs, and in unexpected standstill during anesthesia, surgery, and other therapeutic and diagnostic procedures.

After emergency resuscitation, intrinsic ventricular activity at times fails to reappear promptly, whereupon continued stimulation is necessary to maintain the heart beat. Under these circumstances, external stimulation has been applied continuously for as long as 16 days. During this period, while the patient is being kept alive by electric stimulation, attempts can be made to arouse intrinsic ventricular activity with the careful, deliberate use of sympathomimetic amines. For this purpose, the intravenous administration of dilute solutions of epinephrine and isoproterenol has been found to be most effective and safe.

Finally, external electric stimulation has also been found valuable in patients with Stokes-Adams disease to prevent abnormal ventricular irritability, ranging from multifocal beats to tachycardia and fibrillation (fig. 2). We have demonstrated repeatedly that acceleration of the ventricular rate above a critical level, whether by electric stimulation or by sympathomimetic amines, will prevent these manifestations of ventricular irritability and maintain a regular ventricular rhythm. The critical levels above which ventricular irritability is controlled vary somewhat from patient to patient and from time to time in the same patient; they usually range between 40 and 60 beats per minute but are occasion-

From the Medical Research Department, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

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Emergency resuscitation from ventricular standstill by external electric stimulation. Continuous electrocardiogram (lead aVp at half standardization) from patient with Stokes-Adams disease shows at first complete heart block with idioventricular beats (R) followed by ventricular standstill. Electric stimuli (E) terminate the standstill by producing ventricular responses (V). A spontaneous idioventricular beat (the first R in the fourth row) interrupts the regular externally paced rhythm; the next stimulus does not produce a ventricular response because it falls in the refractory period. With cessation of stimulation the idioventricular pacemaker resumes control.

Characteristics of Electric Stimuli

Extensive experimental and clinical experiences have indicated the optimal features of the electric stimuli (fig. 3). Monophasic, rounded waves were found to be more effective than a variety of other monophasic and biphasic wave forms (sinusoidal, spike, and rectilinear). A duration of 2 to 3 milliseconds has been found to be most effective and safest: shorter impulses require larger currents to stimulate the heart; longer impulses do not significantly lower the current required and increase the risk of multiple responses to a single stimulus. The current and voltage of effective stimuli ranged in our patients from 50 to 200 milliamperes and from 15 to 100 volts.

Technic of Application

The pacemaker is attached to the patient by two output wires connected to circular electrodes, 3 cm. in diameter. The electrodes are placed over the precordium, one at or outside the cardiac apex (V4 to V6 position) and the other to the left of the sternum at or above the apical level (V2 to V4 position). The electrodes may be moved and their polarity may be reversed to find the lowest threshold of stimulation and the clearest electrocardiographic recording. The electrodes should be moved and cleaned several times a day to minimize local skin irritation. Good electric contact is made with electrode paste or jelly, and the electrodes are held in place with plas-
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Prevention of ventricular fibrillation by external electric stimulation. Continuous electrocardiogram (lead aV_{F} at half standardization) shows that stimuli (E) at 60 per minute (1.04-second interval) maintained a regular ventricular rhythm. When stimulation was slowed to 50 per minute (1.21-second interval), multifocal ventricular activity broke through and culminated in a paroxysm of ventricular fibrillation. Continued stimulation had no effect but the fibrillation stopped spontaneously. Then stimuli at 70 per minute (0.84-second interval) restored regular ventricular rhythm. (Reproduced with permission of the publisher from New England Journal of Medicine 262:108, 1960.)

Figure 2

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there is not time to attach an electrocardiograph. In the absence of an electrocardiogram, however, resuscitation of the patient or palpation of synchronous pulses is satisfactory evidence of the efficacy of stimulation.

**Untoward Effects of External Stimulation**

No untoward cardiac effects of external electric stimulation have been observed. Bursts of multifocal ventricular beats, ventricular tachycardia, or ventricular fibrillation have not been produced. We have found no evidence of damage from the electric current to the heart or to neighboring structures at necropsy.

The major untoward effects are chest pain and muscular twitch. The intensity of the pain and of the muscular contraction varies in different patients; in some it is negligible, in others it makes continued stimulation difficult. Meperidine (Demerol) hydrochloride or paraldehyde usually makes the discomfort tolerable and permits continued stimulation. Local infiltration with procaine hydrochloride under the electrodes does not reduce the pain. With prolonged stimulation the severity of the pain usually diminishes markedly and less

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**Figure 3**

*Optimal electric features for external cardiac stimulation and countershock.*

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**Figure 4**

*Electrocardiographic demonstration of the effectiveness of external electric stimulation. Lead aV_F at half standardization. A. Electric stimuli (E) are increased in intensity until they produce ventricular responses (V) which replace the slower idioventricular beats (R). B. Variations in the rate of stimulation produce corresponding variations in the rate of responses. C. Interruption of stimulation is followed by a ventricular pause of 4.64 seconds before intrinsic ventricular beats reappear. D. With a longer pause electric stimulation is resumed. (Reproduced by permission of the American Heart Association, Inc., from Circulation 9:486, 1954.)*
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medication is required. The muscular twitch is greatly reduced by curariform drugs. The only tissue damage from electric stimulation has been superficial ulcerations under the chest electrodes in patients treated for a day or more. This problem has been minimized by frequent small changes in the positions of the electrodes and meticulous care of the skin. Flexible adhesive or soft rubber electrodes greatly reduce skin trauma; though useful for long-term monitoring, they are unsuitable for stimulation because of the relatively high electric resistance.

**Cardiac Monitoring**

Crucial to the successful resuscitation of patients from cardiac arrest is prompt recognition of the onset of the emergency. The interval between circulatory arrest and the resumption of effective ventricular output must be brief, less than 3 or 4 minutes, if cerebral and cardiac function is to return unimpaired. Cardiac arrest may pass unrecognized and untreated in unattended or anesthetized patients unless a cardiac monitor immediately signals the emergency.

Ideally, a cardiac monitor should be easy to apply, should give an audible alarm with the onset of arrest, should demonstrate the mechanism of arrest, whether ventricular standstill or fibrillation, and should be combined with a pacemaker to provide means of immediate, even automatic external electric stimulation in case of standstill. Such monitors are used to great advantage in patients in whom there is a special threat of cardiac arrest, as in acute myocardial infarction, Stokes-Adams disease, anesthesia, cardiac arrhythmias, and cardiac catheterization.

**Program for Cardiac Arrest**

Equally important to the success of resuscitation is the prompt institution of a prearranged and well-rehearsed program of action (table 1). The emergency restoration of circulation may involve external electric stimulation for ventricular standstill, external electric countershock for fibrillation, manual blows to the precordium, external cardiac massage, cardiac puncture, and, in appropriate circumstances, even thoracotomy with direct cardiac massage. The sequence of the procedures depends upon their relative safety, speed of applicability, and mechanism of the arrest. Artificial respiration may also be necessary in the event of respiratory arrest.

After circulation has been restored, two additional problems may arise: effective intrinsic cardiac rhythm may not return promptly, and cardiac arrest may recur. The permanent prevention of recurrent episodes is a specially difficult problem in Stokes-Adams disease and often requires long-term direct cardiac stimulation with internal electric pacemakers.

**Direct Cardiac Stimulation**

**Indications**

Long-term electric stimulation of the heart is valuable for the complete prevention of recurrent Stokes-Adams attacks, which are often not controlled by drugs. External stimulation is unsatisfactory for the long term because of pain and skin irritation. Direct

<p>| Table 1 |</p>
<table>
<thead>
<tr>
<th>Program for Cardiac Arrest</th>
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</thead>
<tbody>
<tr>
<td>1. Emergency restoration of circulation</td>
</tr>
<tr>
<td>Precordial blow</td>
</tr>
<tr>
<td>External electric stimulation or countershock</td>
</tr>
<tr>
<td>External cardiac massage</td>
</tr>
<tr>
<td>Cardiac puncture and intracardiac epinephrine</td>
</tr>
<tr>
<td>Thoracotomy and massage</td>
</tr>
<tr>
<td>if other methods fail</td>
</tr>
<tr>
<td>if adequate help is available</td>
</tr>
<tr>
<td>if prognosis is favorable:</td>
</tr>
<tr>
<td>no irreversible cerebral damage</td>
</tr>
<tr>
<td>general condition good</td>
</tr>
<tr>
<td>Artificial respiration</td>
</tr>
<tr>
<td>2. Restoration of intrinsic cardiac rhythm</td>
</tr>
<tr>
<td>Electrocardiograph or monitor</td>
</tr>
<tr>
<td>Electric stimulation or countershock</td>
</tr>
<tr>
<td>Drugs: epinephrine, isoproterenol, procaine amide, calcium salts, norepinephrine, sodium bicarbonate</td>
</tr>
<tr>
<td>3. Prevention of recurrent episodes</td>
</tr>
<tr>
<td>Cardiac monitor</td>
</tr>
<tr>
<td>Intravenous epinephrine, isoproterenol, atropine</td>
</tr>
<tr>
<td>Oral ephedrine and isoproterenol</td>
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<tr>
<td>Internal electric pacemaker</td>
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cardiac stimulation with electrodes on or in the heart requires current of low intensity and obviates these difficulties. For assured prevention of seizures, whether due to ventricular standstill or fibrillation, the unreliable intrinsic ventricular pacemaker can be replaced by a reliable electric one to drive the ventricles continuously and indefinitely (fig. 5). The unpredictable occurrence of Stokes-Adams attacks and the variable effects of drugs on them make it difficult for the physician to determine the risk of recurrent episodes in comparison with the risk of surgery and to decide whether to pursue drug therapy or to implant an electric pacemaker. Conditions that influence the decision to operate include the age and physical condition of the patient; the frequency, severity, and etiology of the seizures; and the effects of previous therapy. For example, surgery should be undertaken promptly in a vigorous, 60-year-old man suffering from frequent severe Stokes-Adams attacks that are without apparent reversible cause and are uncontrolled by drugs. On the other hand, a prolonged trial of drug therapy would seem appropriate in a feeble, elderly patient whose attacks stopped when drugs were administered.

Long-term stimulation at normal rates is also beneficial for patients with heart block who suffer from diminished cardiac output and congestive failure due to slow ventricular rates.

Methods of Placing Electrodes

Direct stimulation can be accomplished by placement of electrodes in the myocardium at open thoracotomy or by blind percutaneous puncture, or by introducing a catheter electrode into the right ventricular cavity by way of a peripheral vein. Although it seems sim-

Figure 5
Direct cardiac stimulation by implanted pacemaker. Lead 1. Top. Complete heart block and slow idioventricular pacemaker (R) before surgery. Middle. Electric stimuli (E) from the artificial pacemaker produce regular ventricular responses (V). Bottom. Competition between conducted sinoatrial beats (R) and the artificial pacemaker. A fusion beat follows the third electric stimulus. (Reproduced with permission of the publisher from Annals of Surgery 154:340, 1961.)
plest, placement of a myocardial electrode by blind percutaneous puncture is not useful clinically because it is difficult to accomplish and maintain, and it carries the risks of damage to a coronary vessel, pericardial tamponade, ventricular fibrillation, infection, and ineffective stimulation.

Endocardial catheter electrodes provide a means of direct cardiac stimulation without the need for thoracotomy. Although this approach has been used for the long-term control of Stokes-Adams disease, infection, thrombosis and embolism, cardiac perforation, cardiac arrhythmia, and ineffective stimulation due to movement or breakup of the catheter seem to us to make it unsatisfactory. Nevertheless, it is very useful as a temporary, relatively simple means of cardiac stimulation for a few days. This approach permits assessment of the effects of various rates on the cardiac output and on the prevention of seizures, and with the resultant improvement in the patient's condition more definite treatment may be undertaken.

The heart may be stimulated by way of the catheter electrode at any desired rate over a greater range than can be accomplished safely with sympathomimetic drugs, although they are usually effective in preventing seizures and in accelerating the ventricular rate adequately. The pharmacologic approach has the advantages of being simple, quickly applicable, free from the hazards inherent in the catheter technic, and safe if carefully controlled. The need of close observation for adequate control is its major drawback. We consider this difficulty to be more acceptable than the hazards of the catheter electrode, and, accordingly, we have usually chosen the pharmacologic technic for the short-term control of Stokes-Adams attacks.

The catheter electrode presents a significant risk of ventricular fibrillation, as does any electrode that connects the heart directly with the external surface of the body. Small and ordinarily unrecognized currents may produce ventricular fibrillation, if they accidentally reach the heart by such a pathway. Such small currents may leak from improperly grounded electrical instruments (electrocardiographs, oscilloscopes, galvanometers, pacemakers, defibrillators). These currents may reach the heart by direct connection of the instrument to the cardiac electrode and even by indirect contact across the moist skin.

Implantation of myocardial electrodes at open thoracotomy remains the procedure of choice for long-term direct cardiac stimulation.

**Myocardial Electrodes**

Early attempts at direct stimulation of the heart by electrodes placed in the myocardium at thoracotomy failed within a few weeks because the threshold for stimulation rose progressively. This difficulty resulted not from polarization or other effects of the electric stimuli but from tissue reaction to the foreign body, which in effect separated the electrodes from excitable myocardium. This problem of the rising threshold was first solved with electrodes of stainless steel and later with other nonreactive materials, particularly platinum and platinum iridium, and by meticulous avoidance of contamination of the electrodes and the site of implantation with foreign particles of any kind.

The second problem that arose with myocardial electrodes was occasional breakup of the electrode itself or the connecting wires. Chardack has discarded the stainless-steel electrodes he used initially and developed new ones of platinum-iridium coil insulated with silicone rubber with which he has reported excellent results but which still break at times. At present, we prefer electrodes made of special, twisted strands of stainless steel, electroplated with gold and platinum, and insulated with Teflon. These new electrodes combine mechanical strength with inertness; there has been only one broken wire and no other failure in 26 new systems, all implanted in the last 8 months. With our technic, thresholds for stimulation, which usually start between 0.1 and 1.0 milliampere, reach a final level of 2.0 to 4.0 milliamperes within a month. Clinical experiences are still
too short, however, to provide final evaluation of the problems of wire breakage in relation to the many years that patients may need reliable systems.

**Power Supply**

Initially, the myocardial electrodes were connected by wires that traversed the skin\textsuperscript{29,30} to an externally carried pacemaker powered by easily replaceable batteries. This technic proved unsatisfactory for long-term use because of infection and wire breakage, so that pacemakers were developed that could be placed subcutaneously.\textsuperscript{31,32}

Several ways of providing power for internal pacemakers have been developed. At present, we prefer miniature pacemakers\textsuperscript{*} containing batteries that provide electric stimuli 2 milliseconds in duration, of 7 volts and 14 milliamperes, and at rates about 72 per minute (fig. 6). Such stimuli are of optimal duration and of sufficient voltage to give currents with a wide margin of safety above threshold. With this drain of energy the batteries are expected to last about 5 years. Then a fresh instrument can be substituted in a minor procedure. Chardack\textsuperscript{33} has provided special controls in the instrument whereby the rate and voltage can be varied after implantation by needles inserted percutaneously. It remains to be seen whether the prolongation of battery life, resulting from adjustment of the stimulus voltage just above threshold, and the variability of rate are worth the reduced margin of safety, the added complexity of the instrument, and the risk of infection.

It is possible to use batteries in the implanted pacemaker that can be recharged periodically from a radio-receiver or secondary induction coil activated from an external power transmitter. Such a pacemaker has been developed and used clinically.\textsuperscript{35} The output of the instrument, however, was only 2 volts, and it failed in several cases. This approach, therefore, cannot be considered ready for clinical application.

To avoid an internal power source that ultimately requires replacement, energy can also be transmitted across the skin by radiofrequency signals or by induction from external transmitters with easily replaceable batteries.\textsuperscript{3,36-39} Such approaches have the additional advantages of requiring relatively small receivers and of permitting ready variation in rate of stimulation. Furthermore, in some modifications\textsuperscript{38,39} the receiver has been fixed directly to the myocardium with the idea of eliminating breakage by removing the wires between the myocardial electrodes and the receiver; unfortunately, breakage of the stiff myocardial pin electrodes remains a problem.\textsuperscript{39} The energy requirements of all these systems are such that either the transmitter must be in close apposition to the subcutaneous receiver or the power source must

\textsuperscript{*}Manufactured by Electrodyne Company, Norwood, Massachusetts.
be so large as to hinder normal activity. With these limitations, reliable continuous stimulation of the heart for assured prevention of Stokes-Adams attacks does not seem to us to be practical. An ordinary bath or shower, for example, is difficult. The first case reported by Cammilli\textsuperscript{38} presents a striking example of the unacceptable ease with which stimulation from external devices may be interrupted: this patient died of cerebral damage consequent to ventricular fibrillation that occurred when the transmitter was removed temporarily by a physician in the hospital. Furthermore, preoccupation and anxiety over the equipment create a psychologic hindrance to the normal activities of life.

It has been suggested that stimulation be applied only intermittently as needed, to be turned on automatically or by the patient.\textsuperscript{37} Automatic triggering would require complicated feedback systems and is technically impractical at present. Control by the patient appears unwise because of the unpredictability, abruptness, and lethal potentiality of Stokes-Adams attacks.

**Rate of Stimulation**

Continuous long-term stimulation at a fixed predetermined rate regardless of the presence or absence of intrinsic ventricular activity has proved a practical and satisfactory solution to the major problems presented by heart block and Stokes-Adams disease. Suppression of intrinsic ventricular activity or competition between the artificial pacemaker and the sinoatrial pacemaker if atrioventricular conduction returns (fig. 5) does not create clinical difficulties. Irregularity of rhythm may occur with this artificial parasystole but it has not been of clinical significance in our 19 patients in whom it occurred. Although innumerable stimuli have fallen in the vulnerable phase, repetitive responses and ventricular fibrillation have not been produced. Experimental observations also indicate that stimuli of 2 milliseconds' duration and of the strengths used for direct stimulation do not produce ventricular fibrillation no matter when they fall in the cardiac cycle.

Although variability of the rate of stimulation may seem advantageous, selection of a fixed rate makes for greater simplicity and reliability, and for smaller size of the pacemaker. For longest battery life it is desirable to set the rate as low as possible consistent with satisfactory cardiac output and prevention of seizures. The usual intrinsic idioventricular rates of 25 to 45 beats per minute in patients with complete heart block are ordinarily adequate to prevent cerebral symptoms and are compatible with normal activity for many years. Functionally, however, such rates are insufficient in that cardiac hypertrophy almost invariably occurs, and limitation of exercise tolerance and congestive failure often develop. Cardiac acceleration is the primary mechanism by which cardiac output is increased. With excessive acceleration, however, the cardiac output no longer increases; driving the heart at fixed rates between 60 and 100 beats per minute seems to provide an optimal cardiac output.\textsuperscript{40, 41} A pacemaker system has been developed that does allow the patient to vary the rate.\textsuperscript{42} The added complexity of the instrument and the requirement that the patient manipulate externally carried apparatus seem both unnecessary and undesirable to us. Our patients with a fixed rate of 70 to 75 per minute can carry out normal activity and exercise without difficulty. Rates about 70 were also found effective in preventing recurrent ventricular tachycardia and fibrillation;\textsuperscript{32} rates of 60 or less\textsuperscript{33} may be too close to the critical rate\textsuperscript{5} to be reliable for this purpose.

A number of workers have suggested the desirability of driving the ventricles at the variable sinoatrial rate and with a normal atrioventricular sequence rather than at an arbitrary fixed rate with complete atrioventricular dissociation.\textsuperscript{43-45} The ventricular rate would then vary in response to physiologic stimuli and would provide appropriate changes in cardiac output, as during sleep, exercise, and fever. Furthermore, the normal sequence and timing of atrioventricular excitation and contraction would restore
the contribution of atrial systole to ventricular output.45 Ventricular output is said to increase 10 per cent or more due to increase in initial intraventricular tension and to normal closure of the atrioventricular valves. As demonstrated by Butterworth and Polindexter,46 atrial impulses can be made by electronic means to stimulate the ventricle. These systems involve two sets of wires on the myocardium (atrial and ventricular), amplifiers, delay circuits, impulse generators, and power sources. In addition, safeguards are perforce included to prevent excessive ventricular slowing or tachycardia in response to atrial arrhythmias. A system of this sort small enough to be implanted has recently been developed and used in man.45 Such a system is necessarily larger and more complex than one with a fixed rate. The disadvantages of increased complexity with consequent increased risk of component failure, of larger size, and of increased power requirement with consequent shorter life of the instrument must be balanced against the small and ordinarily inconsequential increase in cardiac output and refinement in physiologic function. It should be kept in mind that the primary purpose of artificial pacemakers is to provide completely reliable prevention of Stokes-Adams attacks; this basic objective should not be compromised for secondary gains.

Results

Implantation at open thoracotomy of myocardial electrodes and subcutaneous pacemakers is the most widely used and successful technic for long-term electric stimulation of the heart. Many hundreds of patients ranging in age at least from 3 to 82 years have been so treated, mostly for Stokes-Adams attacks. In our own experience pacemakers have been implanted by Dr. Howard A. Frank in 53 patients, 52 for Stokes-Adams attacks and one for congestive heart failure. There has been one postoperative death, from pulmonary insufficiency. Four other patients have died from infection and cerebrovascular disease, from a Stokes-Adams attack following wire breakage, and from unexplained hypotension; the fourth patient died suddenly without apparent cause even though the pacemaker system was functioning perfectly. The deaths due to infection and wire breakage occurred early in the series; these complications have not arisen in the last 29 cases. The remaining 48 patients are free from Stokes-Adams attacks and have been able to resume normal activity.

Physiologic Observations

Electric stimulation of the heart, both external and direct, has provided opportunities for physiologic and pharmacologic studies, many of which have previously not been possible in man, and has led to revived interest in heart block and Stokes-Adams disease in the last decade. Such studies have included the relation of heart rate to cardiac output,40, 41 effects of sympathomimetic amines on ventricular rhythmicity and atrioventricular conduction,12 depression of idioventricular pacemakers by rapid stimulation,47 delineation of refractory and supernormal periods of ventricular excitability,48 features of antegrade and retrograde atrioventricular conduction,49 and an analysis of fusion beats.50 Advances in our knowledge of cardiac physiology, particularly in relation to arrhythmias, must surely come from such observations, which have their origin in this new electrical approach to the treatment of this long-recognized, somewhat uncommon, and still poorly understood disease.

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References


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32. ZOLL, P. M., FRANK, H. A., ZARSKY, L. R. N.,


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