ELECTROCARDIOGRAPHIC STUDIES DURING ENDO-
TRACHEAL INTUBATION. V. EFFECTS DURING
GENERAL ANESTHEIA AND HEXYLCAINIA
HYDROCHLORIDE TOPICAL SPRAY

RAYNOLD A. ARCURI, M.D.,† W. NEWMAN, M.D., AND CHARLES L. BURSTEIN, M.D.

BRONX, N. Y.

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In previous communications it was found that the incidence of electro-
cardiographic disturbances during endotracheal intubation under gen-
eral anesthesia could be reduced from over 60 per cent to about 17 per
cent with procaine given intravenously and to 12 per cent with diethyl-
aminoethanol or procaine amide, respectively, administered intrave-
rously prior to intubation (1–4). During the course of these investiga-
tions it was noted that topical cocainization of the pharynx and larynx
seemed to enhance cardiac disorders, producing especially ventricular
premature contractions. In an effort to overcome this peculiarity of
cocaine to sensitize cardiac automatic tissue through stimulation of
the sympathetic nervous system while retaining the beneficial features
of local anesthesia, other topical agents have been tried. Unfortunately,
some of these are also toxic in their own right, stimulating the central
nervous system or depressing circulation.

A new local anesthetic agent, "cyclaine®," has been under investiga-
tion for some time and seems to be associated with a low index of
toxicity as well as good topical anesthetic properties (5, 6). Cyclaine
is hexylcaine hydrochloride (1-cyclo hexyl amino 2-propyl benzoate
hydrochloride), with a molecular weight of 297.85, and is freely soluble
in water. A 1 per cent aqueous solution has a pH of 4.4 (unbuffered)
and is stable under conditions of boiling and autoclaving. It has been
used in spinal and regional anesthesia but has not been widely used as
a topical anesthetic agent. Studies indicate that it possesses an order
of toxicity comparable to that of procaine and neostesin, and an order
of topical anesthesia comparable to that of cocaine and butacaime.

Method

Spraying the pharynx and larynx, including the epiglottis, vocal
folds and rima glottidis but not the trachea proper, with approximately

* From the Anesthesia Section of the Surgical Service and the Cardiac Section of the
Medical Service, Veterans Administration Hospital, Bronx, N. Y.
† Now attending Anesthesiologist, Mount Vernon Hospital, Mt. Vernon, N. Y.
5 cc. of a 5 per cent aqueous solution of cyclaine after induction of general anesthesia forms the basis of this study. No instance of toxicity of the central nervous system or sympathetic nervous system was noted.

Control electrocardiograms of the first 3 standard leads were obtained in all patients before anesthesia was started. Subsequent lead II electrocardiographic tracings were taken (1) during light surgical anesthesia, (2) during exposure of the glottis and spraying, (3) at the moment of intubation, three to six minutes after spraying with cyclaine, and (4) three to five minutes after intubation. Tracings were made in 50 patients who were to undergo surgical intervention in whom endotracheal intubation was a desired procedure. Cases were not selected as to risk, disease or presence or absence of existing heart disease or arrhythmias. An attempt was made to intubate on the light side, that is, upper or middle second plane.

Results

Cyclopropane-Ether Series.—In 20 patients, anesthetization was accomplished with cyclopropane and ether. Eleven of this number had regular sinus rhythm at the time of intubation or afterward. It is noteworthy that of these, in 2 cases a shifting pacemaker (fig. 1), in 3 cases a sinus bradycardia, in 2 cases a sinus tachycardia, and in one

![Image of electrocardiograms](image-url)
case a regular sinus rhythm with nodal premature contractions (fig. 2) reverted to regular sinus rhythm after spraying with cyclaine, and the regular sinus rhythm was then maintained at the time of intubation. Similarly, in one case the control electrocardiogram, which was normal, was converted to a first degree heart block 3:2, with Wenckebach phenomenon and rare ventricular premature contractions. Following cyclaine spray, this reverted to regular sinus rhythm which was maintained during and after intubation (fig. 3).

In 7 cases, the only change seen at intubation was a sinus tachycardia, but in 3 of these, this rhythm existed before induction.

![Fig. 2. Clearance of nodal premature contractions during cyclopropane-ether anesthesia following topical spray of larynx with 5 per cent cyclaine solution. a. Control electrocardiogram, lead II showing regular sinus rhythm at a rate of 90 per minute. b. During second plane cyclopropane-ether anesthesia, the electrocardiogram shows nodal premature contractions. The glottis and larynx were sprayed with 5 cc. of 5 per cent cyclaine immediately following this tracing. c. Four minutes later, before and during endotracheal intubation, the tracing shows a regular sinus rhythm. d. Three minutes after intubation, no change.

In one case, a regular sinus rhythm was maintained at the time of intubation but a bigeminal auricular premature contraction developed afterward.

In one case, a first degree heart block was converted into a complete heart block at the time of intubation.

This leaves 14 of 20 cases which showed no change from the basic rhythm and 4 additional cases with only the development of sinus tachycardia, not usually considered an ominous arrhythmia.
Cyclopropane Series.—Anesthetization was carried out with cyclo-
propane alone in 11 patients.

Five patients showed no change from a regular sinus rhythm at
the time of spraying, during intubation or afterward.

In 5 patients sinus tachycardia developed after intubation when an-
esthesia was lightening; during the passage of the endotracheal tube
no change was observed. Furthermore, 2 of these 5 patients already
had a preinduction sinus tachycardia and another had an abnormal
electrocardiogram with nonspecific ST and T wave changes.

In only one patient in the cyclopropane series was any type of
serious arrhythmia demonstrated. It is to be noted that in this patient

![Figure 3](image)

Fig. 3. Clearance of first degree heart block with ventricular premature contractions dur-

ing cyclopropane-ether anesthesia following topical spray of larynx with 5 per cent cyclaine®.
a. Control electrocardiogram, lead II showing regular sinus rhythm. b. During second plane
cyclopropane-ether anesthesia, the electrocardiogram shows a first degree heart block, 3:2,

with Wenckebach phenomenon and rare ventricular premature contractions. The larynx was
then sprayed with cyclaine. c. Three minutes after spraying with cyclaine, before and
during endotracheal intubation, the tracing shows a regular sinus rhythm at a rate of 65 per
minute. d. Five minutes after intubation, no change.

an obstruction was present after spraying and the first attempt at in-
tubation resulted in failure. Bigeminal ventricular premature contrac-
tions developed before intubation but were converted to a sinus tachy-
cardia on intubation and reverted to regular sinus rhythm three
minutes afterward (fig. 4).

The remaining 19 patients in this study were anesthetized with vari-
ous other combinations of agents, including pentothal and cyclopropane,
pentothal and curare, pentothal and cyclopropane-ether, nitrous oxide
and ether, pentothal and nitrous oxide, evipal and nitrous oxide-ether.
One patient, while awake, was intubated with 5 per cent cyclaine
topical anesthesia only and then anesthesia was induced with cyclo-
propane and ether.
Fourteen cases showed no change from their basic rhythm. Nine patients with regular sinus rhythm showed no change from regular sinus rhythm. Five of these had sinus tachycardia before induction and this rhythm was maintained during intubation, the rate increasing slightly in three to five minutes.

Of the 5 patients who had changes in rhythm, 2 patients with regular sinus rhythm had sinus tachycardia after intubation. First degree heart block with Wenckebach phenomenon developed in one patient who had sinus tachycardia and a PR interval of 0.2 second. One patient with hypertensive arteriosclerotic heart disease and a history of myocardial infarction had rare nodal premature contractions three minutes after intubation. In one patient with right bundle branch block

![Fig. 4. Clearance of bidirectional ventricular premature contractions during cyclopropane anesthesia with obstruction following topical spray of larynx with 5 per cent cyclaine®.](image)

- a. Control electrocardiogram, lead II showing normal regular sinus rhythm.
- b. During second plane cyclopropane anesthesia with respiratory obstruction, the electrocardiogram shows bidirectional premature ventricular contractions. The larynx had just been sprayed with 5 cc. of 5 per cent cyclaine.
- c. Two minutes later, during endotracheal intubation, the tracing shows a sinus tachycardia, rate 120 per minute.
- d. Three minutes later, no change.

there was no change during intubation while awake, after topical administration of 5 per cent cyclaine, but slight hypoxia was experienced when anesthesia was induced with cyclopropane and ether, and transient, bigeminal, ventricular, premature contractions developed.

**Comment**

Means generally employed to abolish arrhythmias during intubation include deepening the plane of anesthesia, or adding such cardiac depressors as quinidine, procaine or procaine derivatives, or a combination of both. Some investigators have tried to protect the patient by intravenous administration of barbiturates. Unfortunately, either pulmonary ventilation is depressed, often to such a degree as to bring in the factors of oxygen lack and carbon dioxide retention, or the addi-
tion of depressants produces undesired changes. To obviate these disturbing features an attempt was made to approach the problem by removing the afferent arc of the reflex by which it is thought such arrhythmias are produced. Cocaine, although an efficient topical agent for this purpose, may in itself be toxic to the cardiovascular system. Previous observations have shown that not only circulatory depression and collapse but serious arrhythmias may result when cocaine is used in this connection. Preliminary studies have shown that 5 per cent aqueous solution of cycaine possesses adequate topical anesthetic properties for the larynx (7). In our experience this is confirmed and is associated with a low order of toxicity. Furthermore, cycaine is unique in that it apparently has qualities similar to those of procaine in its anti-arrhythmie effects. This is well illustrated in the accompanying illustrations (fig. 1 to 4). The comparative incidence of arrhythmias when cocaine was utilized in other series was not significantly diminished when compared with the incidence following intubation without topical anesthetization. For example, in one group of 40 cases, various abnormal cardiac rhythms were noted in 31. By contrast, when cycaine was used, the over-all incidence of arrhythmias was 30 per cent, and the actual incidence during intubation was 14 per cent.

Summary

Electrocardiographic tracings were obtained in 50 adult patients who were given general anesthesia complemented by topical anesthetization of the pharynx and larynx with a 5 per cent aqueous solution of cycaine. Electrocardiographic disturbances occurred in 14 per cent of the cases at the time of intubation. This incidence compares favorably with that in the previous series, including those in which procaine, diethylaminoethanol and procaine amide were used prior to endotracheal intubation. In the series in which procaine or its derivatives had been omitted under similar conditions the incidence of such disturbances was more than 60 per cent. Past experience has not helped to reduce the frequency or severity of these arrhythmias by using cocaine as a topical anesthetic agent. Cycaine, a clinically new local anesthetic agent with adequate topical anesthetic properties, has been found to be free from sensitizing effects and, in addition, to possess a procaine-like action in actually clearing some arrhythmias produced.

Acknowledgment

The cycaine® used in this study was obtained from the Medical Research Division of Sharp and Dohme, Inc., West Point, Pa.

References


7. Clark, Robert E., Personal communication to author.

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Thursday, April 9, 1953

Pharmacology of Autonomic Blocking Agents—Mark Nickerson, Ph.D., M.D., Associate Professor of Pharmacology, University of Michigan School of Medicine, Ann Arbor.

Reflex Changes During Anesthesia—E. M. Papper, M.D., Executive Officer of the Department of Anesthesiology, College of Physicians and Surgeons, Columbia University; Director of the Service of Anesthesiology at the Presbyterian Hospital, New York, N. Y.

Management of Anesthesia Associated with the Autonomic Nervous System—Harvey Slocum, M.D., Professor and Chairman, Department of Anesthesiology, University of Texas, Medical Branch, Galveston.

Commissurotomy: The Effects of the Autonomic Nervous System and Their Management—Harold Miller, M.D.

Nerve Sympathomimetic and Parasympathomimetic Agents—Mark Nickerson, Ph.D., M.D.

Nerve Injuries Incident to Anesthesia—Morris J. Nicholson, M.D., Department of Anesthesiology, Lahey Clinic, Boston.

Diagnostic and Therapeutic Uses of Regional Anesthesia—Frederick P. Haugen, M.D., Associate Professor of Surgery, Head of Division of Anesthesiology, University of Oregon Medical School Hospitals and Clinics, Portland, Oregon.

Round Table—Diagnostic and Therapeutic Uses of Regional Anesthesia.

E. M. Papper, M.D.—Moderator
Frederick P. Haugen, M.D.
John J. Bonica, M.D.
Daniel C. Moore, M.D.
J. Samuel Denson, M.D.
Horace B. Graves, M.D.

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