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Curare as an aid
to the Anaesthetist.

by

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It is now more than three years since we first began to use a purified extract of the old drug curare as a muscle relaxant ⁽¹⁾ in patients under general anaesthesia.

~~It is gratifying that~~ Numerous reports from ~~many~~ anaesthetists throughout the world are confirming our original surmises as to the clinical efficacy and safety of this application of curare. I believe that it is now possible to make ^{at least a} preliminary appraisal of the true place of curare in anaesthesiology, and I propose briefly to discuss the drug under the following headings:

- 1 The need for curare
- 2 The efficacy of curare
- 3 The safety of curare
- 4 The effect of curare on the future practice of anaesthesiology

1. Need. Every anaesthetist ^{even the most} ~~so~~ ⁽²⁾ expert, has wished at times that there was some way in which he could instantly and safely produce complete muscular relaxation in his patient. Muscle relaxation is ^{often} a prime requisite for good surgery and to obtain adequate relaxation the anaesthetist may ~~be~~ ^{be} forced to use ~~the~~ anaesthetic drugs, either general or regional, in doses beyond the optimum for the safety and comfort of the patient. It was the need for a drug which would produce controllable relaxation without added toxicity which led us to experiment with Curare in anaesthesia.

2. Efficacy. The purified extract of curare which was introduced into clinical medicine in 1940 by E.R. Squibb & Sons of New York under the name of "Intocostin" was first used in neuro-psychiatry and its major application before ~~its~~ its use in anaesthesia was for the

by Bennett of Nebraska for the
minimizing of trauma in patients (3)
undergoing convulsive shock therapy.

This led us to a cautious trial in patients
under cyclopropane anaesthesia, and
from the very first patient it became
obvious that here was an efficient drug ~~for~~
^{to} ~~relaxation~~ with ~~apparently~~ few side effects. The
~~dosage and method of administration~~
~~has been~~ have varied widely with
different investigators. Some anaesthetists,
notably Cullen of Iowa, have given
curare routinely in all abdominal
operations under general anaesthesia,
usually by ~~fractional~~ repeated intravenous
injections ~~as the need~~ of small doses
of 40 to 60 mg. (2 to 3 cc of "Datocostin")

~~This practice has~~ Knight and
Baird of Minneapolis have also
reported successful series of
administrations using this
technique. My own practice
has been to administer curare
only when there is need to obtain
increased muscular relaxation

④

This may be done at any time during the operation and should be in adequate dosage ~~2 to 5 cc~~ (60 to 100 mg. for an adult ~~♂~~ under cyclopropane), but is by no means necessary in every abdominal ~~operation~~ case. A recent survey of our own cases shows that, although we now use Curare on the slightest provocation, we still are administering it in only 38% of our abdominal operations. Curare should not be made the excuse for a poor anaesthetic sloppily administered.

For many years it has been my own practice to use cyclopropane as the agent of choice for general anaesthesia to the almost complete exclusion of ether. For this reason most of my work with Curare has been with

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patients under cyclopropane anaesthesia. The two drugs seem to make an ideal combination and enable us to obtain at will relaxation similar to that of spinal anaesthesia. Curare may also be used in ether anaesthesia or when ether is combined with cyclopropane, ethylene or nitrous-oxide, but as Bullen ~~has shown~~ the under these circumstances the dose of curare should be greatly reduced - to an average of 20 to 40 mg (1 to 2 cc of Introcotin) for an adult. Bullen has shown that ether itself has a curare-like action on the myo-neural junction, and which accounts for the greatly enhanced effect of curare in patients under ether anaesthesia. Macintosh, of Oxford, is using ^{small doses of} curare successfully in patients under light ether, administering it by continuous sternal drip.

Curare may also be used (6)
with other anesthetic agents.

Waters reports ~~low~~ satisfactory
anesthesia for upper abdominal
surgery using Curare in combination
with nitrous oxide-oxygen without
added ether. I have frequently
given Curare to patients under
ethylene or ethylene-cyclopropane
with good results. Incidentally
I would like to interject a good
word for that almost forgotten
agent ethylene - a particularly
safe anesthetic for use in such
poor risk cases as toxic thyroids,
and made doubly efficient when
combined with Curare -

Hudson, of Quebec, and others
have shown how Curare may
be used to reinforce the action of
pentothal. It may ~~also~~ be
given to patients in whom the
relaxation of spinal anesthesia
is wearing off too soon, provided

that the sensibility of the patient is well obtained by hypnotics or a "sleeping dose" of ~~gas~~ as general anaesthesia.

It may also be used to facilitate bronchoscopy in ~~difficult cases~~ muscular patients, and tracheal intubation in cases where there is difficulty in securing adequate relaxation. However, Curare in ~~recommended~~ ^{safe} doses is not in any sense an anaesthetic agent and I do not recommend it for general use in conscious patients. The effect is too uncomfortable.

My own feeling is that Curare is most effectively used with the gas anaesthetics, especially cyclopropane, and also but more cautiously with ether.

It may be given intramuscularly without irritation, but we prefer to use it intravenously because of the greater control thus assured.

3. Safety. Perhaps the most surprising outcome of the whole curare investigation is the absence of evidence of toxicity, either immediate or post operative. It is hard to believe that a drug which has such a fabulous reputation as a poison could be used so safely in clinical medicine.

The work of [] and a host of physiologists both before and since his time, has all been done with a comparatively crude curare of uncertain composition and ~~containing a variable quantity of other adulterating substances.~~ ~~It was not until the work of Sill in 1938~~

R. C. Sill, an American who had lived for years in the Amazonian jungles of Ecuador brought to civilization in 1938 the prob

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Botanically identifiable supply
of Curare and his work made
it possible for Prof. A.R. McIntyre
of Nebraska, the Research Laboratories
of E.R. Scribb & Sons of New York,
and others to produce the first
pharmacologically standardized
extracts of Curare. This new
product is rapidly broken down in
the human body and completely
eliminated. When administered
intravenously ^{in a simple dose} it acts within thirty
seconds, ^{maintains} attains its maximum
effect for about five or ten minutes
and then gradually disappears
until its effect is all gone in about
twenty minutes. The effect may
be prolonged by a judicious
combination with whatever anesthetic
agent is being administered simultaneously.
This rapidity of elimination from
the ~~body~~ ^{body} is undoubtedly the

greatest safety factor in the use of curare in anaesthesia

The question of ^{what is} the optimum dose and what will happen when an overdose is given has been the subject of some ^{interesting} recent reports.

~~Whitace~~ During anaesthesia ~~is~~ a small proportion of patients the administration of what is considered an average dose of curare will occasionally cause the patient's respiration to become very shallow or to cease. This is because of the paralyzing effect of the drug on the accessory muscles of respiration and finally on the diaphragm. All ~~that~~ the treatment that is necessary is to ~~maintain~~ ~~the~~ carry on artificial ventilation of the lungs by manual compression of the breathing bag during the few minutes it takes until this ~~case~~

depressing Curare effect passes off. I have never seen even any temporary damage, ^{resulting} to the patient. "Prostigmin," a drug which appears to be physiologically antagonistic to Curare, has been recommended as an antidote, but personally I have never needed to use it.

← ^{over} Whitacre of Cleveland, in a most important recent article, records the results of experiments to ~~determine~~ ^{determine} ~~the~~ ^{the} effect of very large doses of Curare on human subjects. ~~It~~ ^{It} is surprising to observe that He makes the surprising observation that a single intravenous injection of 200 mg. of Curare (10 cc of Anticoastin) or about double the dose I have ever used therapeutically — produces sudden unconsciousness, complete muscular relaxation and apnoea. If artificial respiration ~~is~~ with

Levure may be given to
anemic, frail, or shocked
patients ~~without any~~ apparently
~~harm~~ without jeopardizing their
chances of survival. I have
given effective doses on several
occasions to patients in almost
pulseless condition from ruptured
ectopic pregnancies, and there
are numerous reports of its
efficacy in traumatic surgery.

adequate oxygenation is then maintained, ^{blood pressure,} pulse and circulation are unaffected, but the patient remains unconscious and relaxed.

By repeating the injections of curare it has been possible to perform operations such as a gastrectomy ~~using~~ no other anesthetic agent.

This ~~is a rather~~ ^{involves a} revolutionary ~~aspect~~ ^{view} of the physiological action of curare and is not easily explained, but from the purely clinical viewpoint it is reassuring to know that even such large doses of curare may be given without irreversible effect.

During the recovery period Whitacre's patients showed some tendency to bronchospasm, increased ~~pulmonary~~ ^{bronchial} secretion and other undesirable side effects, so that neither he nor I

advocate using curare ~~to~~ ~~produce anaesthesia~~ as a practical method of anaesthesia. We are just glad to know that doses up to 400 mg. have been given to human patients without fatal effect. An even more striking example of an overdose of curare ~~has~~ has been reported by Robson, of Toronto. His patient was an eight pound baby, two weeks old, undergoing operation for a complete diaphragmatic hernia with ether anaesthesia. By mistake a dose of 1 cc of Intocostin (20 mg. curare) was given intravenously to improve relaxation. This was at least fifteen times the recommended dose for such a patient. There was immediate

Complete relaxation and also ⁽¹⁴⁾ complete cessation of respiration. Dr. Robson cleverly maintained artificial respiration with endotracheal oxygen for more than three hours, before there was the least sign of returning muscular activity. In the meantime the surgeon had completed the operation under ideal conditions, and eventually the baby recovered without permanent damage. These case histories tend to reassure us regarding the safety of modern extracts of curare, ~~but they should not blind us~~ when properly used, but I hope they will not blind us to the fact, cause us to forget that when ^{still} improperly used curare is a poison, capable of producing death by respiratory paralysis.

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The only side-effects which we have noted in Curare other than occasional respiratory depression is a transient bronchospasm which developed in three patients immediately following the intravenous injection of moderate doses. This is recorded as a possible effect of Curare, with no suggestion as to the cause — the patients ~~continued under~~ resumed normal breathing within one or two minutes. The preparations of Curare we have used, "Autocostin" and the newer extract "d-tubocurarine" are not irritating to the subcutaneous tissues and there has been no case recorded of phlebitis or other similar complication.

4. Effect of curare on the future of anaesthesiology.

Five years ago when it was first suggested to me by Dr L.H Wright, of New York, that curare might be useful in anaesthesia, I laughed at the idea. I thought about it for ~~a year~~ more than a year, and in January 1942, ~~because no one else had taken up the idea,~~ I tried it out.

Since then I have watched its use spread around the world.

There is no doubt that it is filling a need. Developments in anaesthesia during recent years have been mainly toward increased safety and comfort for the patient. Here is a drug which ~~makes the surgeon~~ allows the surgeon to work more efficiently

without increasing the hazard
 to the patient. ~~an objective~~
~~of patient comfort~~. A most important
 objective in surgical progress.
 It is no wonder that the surgeons
 are enthusiastic supporters of
 the use of curare in anaesthesia.
 I feel now that curare will
 enable us to use the non-toxic
 and controllable gas anaesthetic
 agents, particularly cyclopropane
 and ethylene in a wider
 variety of major operations;
 that it will reduce the use of
 spinal anaesthesia with its
 attendant hazards for upper
abdominal surgery; and that
 it will ~~enable a wider~~ afford
 more efficient anaesthesia with
 low concentrations of ether when
 that agent is chosen.

Opinions about curare vary all the way from that of a leading anaesthetist who states that "curare bids fair to replace not only a great deal of deep ether anaesthesia but a great deal of spinal anaesthesia as well" to the comment of one medical "Columnist," "Why not learn to give an effective anaesthetic?" Personally I am not venturing to ~~the~~ prophesy, but I do know that curare will never take the place of the anaesthetist's skill. ~~The greatest development in modern anaesthesia is not the introduction of new agents and methods but~~ The experience, ability and judgment of the anaesthetist is

more important than any
 new agent or method, and I
 believe that Curare should
 remain as just one more
 good thing in the ~~qualified~~ ^{modern}
 Anaesthetist's ~~modern~~ bag of tricks.
 It is not a plaything for the
 inexperienced.

Summary.

The use of Curare in
 anaesthesia has been reviewed
 with particular reference to its
 efficacy and safety as a
 muscle relaxant in patients
 under ~~general anaesth~~ cyclopropane,
 ether, and other general anaesthetic
 agents. ~~It is considered to be~~
 In the light of more than three
 years clinical experience, it
 is considered to be of value to
 expert Anaesthetists and to be

affording a better surgical 19
field ^{for abdominal operations} with light and non-toxic
anaesthesia. ~~It will probably~~
~~result in~~ It will probably
have a permanent place in
anaesthesiology.

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