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Nature and Effects of Narcotics for Pain

Ralph K. Davies

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CITIZENS OF TODAY'S technical and tense civilization are deluged by advertising of pills such as those that are supposed to prevent sleep on one hand, or induce sleep on the other. A central theme of this advertising is that such pills are "non-habit forming."

From other sources, the public has been made keenly aware of the term *addiction,* and the various ways to, and avenues of, addiction. Addiction usually applies to use of drugs, "dope," or narcotics. The words automatically bring to mind such substances as morphine, codeine, or heroin. The beneficial applications of such compounds have been heralded as a boon to suffering mankind, and rightly so. However, the above-mentioned substances are only a few of many preparations that may be classified as narcotics.

The dictionary defines a *medicine* as a drug that is used to treat diseases, or to relieve pain. This term includes materials that act upon various tissues, organs and systems of the anatomy. Upon further inquiry one finds that the term *narcotic* refers to those preparations which produce profound sleep, lethargy, and relief of pain.

This article will deal primarily with the sensation called *pain,* and the use of narcotics to relieve that sensation.

The term *sensation* refers to the reaction to stimuli of various kinds, which usually are due to our environment. The nerves conduct an impulse along the anatomical structures required, and the reaction produced is a response serving to favorably meet the stimulus. We are all aware of the reflex actions, or "learned" responses, of various parts of our anatomy, to cold, heat, or light. These responses are triggered by anatomical entities labelled *receptors.* Receptors, strangely enough, are strategically located in regions most likely to be so challenged.

However "pain spots" are not so located, and are not specifically designed to detect any particular stimulus. Actually, any condition that may cause potential or actual harm to any tissue may produce the sensation known as pain. There are four general classes of stimuli that will produce pain:

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(1) temperatures above 45° Centigrade
(2) corrosive toxic or caustic chemicals
(3) extreme cold
(4) a great amount of pressure.

The amount or quantity of stimulus required to produce pain—*threshold* (of pain)—surprisingly, is very high. Stimuli that attain the high threshold, and which therefore are capable of producing pain, are said to be *noxious* or *nociceptive*.

Relief of such responses may be brought about by chemical means, or by the application of pressure. Physiologically this entails the "blocking" of a nerve or nervous tissues.

Use of chemicals to block nerves or nerve trunks involves a surgical procedure for surrounding the nerve by some narcotic. More broadly stated, the method may involve inhalation or absorption processes as well. The use of pressure to block nervous impulses is accomplished by inflating sphygmomanometer cuff about the part of the anatomy involved. It is of great interest to note the order or sequence in which sensations disappear in each method. Reports on work done in this area of science may be found in references in physiology and medicine.

Having established what a narcotic is, what factors produce pain, and what general methods relieve pain, let us consider those chemicals that are narcotics, as to their action on our physiology.

Most of the drugs used are of vegetable origin, and a few are classed as inorganic agents, or are of animal origin. The most valuable classification is one based upon the location or tissue upon which action takes place.

Narcotics may either depress or stimulate various tissues. For the most part their depression factor is more useful in relief of pain. Therefore a list of narcotics might well fall into the classes listed below (depressors listed first):

I. Act upon the brain:
   Opium and its derivatives
   Belladonna or similar compounds
II. Act upon the spinal cord:
   Phytostigma
   Strychnine
III. Act upon motor nerves:
   Tobacco

IV. Act upon sensory nerves:
Cocaine

V. Act upon the heart:
Increase in force of heart but decreasing frequency—Digitalis
Decrease force but increase frequency—Aconite

VI. Act upon respiration:
Ipecac

In comparison with the above classification, a chemist would present a list based upon structure of the compounds.

I. Anesthetics:

Ethers (1842; first used by Dr. Crawford Long)

Hydrocarbon residue—oxygen—Hydrocarbon residue

Diethyl ether

$H_3C—CH_2—O—CH_2—CH_3$

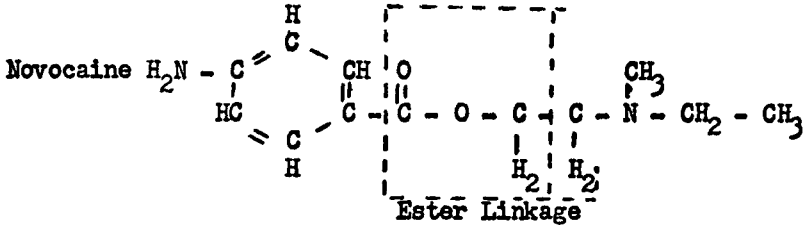
Divinyl ether

Non-ether linkages

Nitrous Oxide N_2O (1846; first used by Dr. Morton, a dentist)

Chloroform $HC\ Cl_3$

Esters (prepared from alcohol and organic acid)



II. Symphathominetics (act upon sympathetic nervous system):

A. Beta Phenylethyl amino group

Epinephrine (historical value) or Adrenaline

B. Phenylisopropyl amino group

Ephedrine

Benzedrine

C. Alcohol

$H_3C—CH_2—OH$

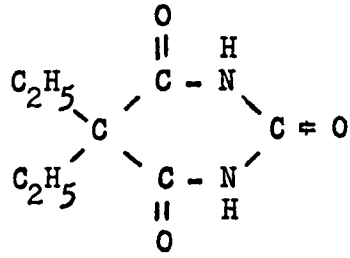
D. Ammonia
NH_3

Basically groups A and B are the derivatives of the benzene molecule (C_6H_6) and appendages of carbon chains plus the nitrogen containing group or "Amino group"

III. Sedatives:

A. Soporifics (sleep producers)
Barbituric Acid structures and derivatives.

Veronal



Phenobarbital

The importance of the above list will be realized when one considers that (1) no one narcotic is perfect, and (2) side effects may present problems to specific patients. Therefore if a basic chemical structure is found (such as those illustrated with "Benzene rings") to be beneficial generally, the molecule may be altered slightly by chemical means, thereby reducing the unwanted side effects. Obviously, a great amount of research and tedious, accurate testing must be carried out prior to the application of the newly constructed drug or narcotic.

Further, it becomes necessary to reconstitute medicinals, as generations of harmful organisms resist previous chemical agents. Consequently many drugs and narcotics are legally available, which are chemical modifications of those known and used for years or even centuries.

At this point it may be fruitful to discuss one narcotic, and to illustrate the ramifications indicated. Let us consider *opium.*

Opium is obtained from a milky substance issuing forth from the cut, unripe capsules of the poppy plant. Turkish opium is the common variety used in the United States, though it also may be found in Asia Minor, Persia, India, and Egypt.

Ether is used to extract the main components of opium for commercial use. This extract will yield some nineteen or more alkaloids, of which the most useful are listed:

I. Those alkaloids related to phenanthrene:
Morphine 2.5—22.8%
Codeine .2—.7%
Thebaine .15—1.0%

II. Those alkaloids related to benzyliso-quinoline:
Papaverine 1.%
Narcotine 1.3—10%
Narceine .1—.7%

Group I alkaloids act upon the central nervous system, as well as stimulate the contraction of smooth muscle.

Morphine $C_{17}H_{19}O_3N$ usually amounts to 9% of opium. In therapeutic doses its narcotic action induces sleep, and relieves pain without causing hypnosis. Physiological processes are depressed, such as mental activity, cough reflex, and constriction of pupils of the eyes. These effects are very pronounced. The tone of the intestinal muscles is increased, and this is accompanied by a decrease in peristaltic activity. The unfortunate property of morphine is that it may be habit forming.

Apomorphine is a dehydrated morphine. The physiological properties of note include cardiac depressant, emetic, expectorant, sedative and hypnotic. Further, a change in the chemical structure decreases narcotic effect, and increases the excitant effect on the central nervous system.

Codeine, which occurs in much smaller quantities, differs from apomorphine chemically by being a methylated (addition of CH_3—methyl groups) morphine. Usually the compound is referred to as a morphine methyl ether. This narcotic is weaker in effect than morphine, but does increase the tolerance to morphine and heroin, although the latter does not reciprocate the property. Codeine is a depressant, an intestinal spasmodic, and a respiratory depressant. Mental depression is not as great as with morphine and therefore addiction potential is not as great. A very common use of codeine is in cough extracts to relieve the dry, irritating cough.

Group II alkaloids derived from opium may be generally characterized by properties of *Papaverine.*

Papaverine $C_{20}H_{21}O_4N$ is a white crystalline solid soluble in water 1: 40. This substance is only slightly narcotic in effect, but it has been observed to increase reflex activity and excitability when administered in large doses. The chief value of this deriv-

ative is that of bringing about relaxation of unstriated (smooth) muscle such as are found in the blood vessels and the gastrointestinal tract. The outstanding properties of papaverine are:

(1) addiction has not been recorded,

(2) no hypnotic effects are known when therapeutic doses are administered.

Obviously, the drugs or narcotics presented above merely illustrate the nature of many others now being used. However, the information of value here is that:

(1) narcotics relieve pain by blocking nervous impulses,

(2) blocking may be accomplished by chemical or mechanical means,

(3) chemical substances may be classified according to the location of their action or the chemical structure of the molecule necessary to produce the narcotic effect, and

(4) knowledge of chemical structure and physiological properties permits the scientist to modify the narcotic, preserving the beneficial effects and reducing the undesirable side effects.