

Morphine was discovered by Sertürner in 1817. Its action is generally similar to that of Opium, it being the principal alkaloid therein, but when used by itself its influence is not complicated with the effects of the convulsive alkaloids (thebaine, codeine and narcotine) which must influence the action of opium to a considerable degree. As compared with the latter, Morphine acts more quickly, and for a shorter time, has less influence on the intestines and skin, is less constipating, less stimulating, less convulsant and less diaphoretic, but more sedative, more anodyne and hypnotic and produces more intense pruritus. Its elimination commences quickly but may not be completed for as much as 48 hours, and is effected by the intestines, the urine, and the salivary glands. It is also eliminated by the gastric mucous membrane, is reabsorbed by the intestinal vessels, and constantly reappears in the stomach until finally excreted. When injected hypodermically more than one-half the amount administered may be recovered by repeatedly washing out the stomach. It is probably retained in the organism to a great extent when the action of the kidneys is defective, and when given continuously in renal disease may accumulate with fatal result.

Apomorphine in dose of gr.  $\frac{1}{10}$  given hypodermically is a systemic emetic, acting directly on the vomiting centre, and is the quickest, most certain and least irritating of all emetics, acting in about ten minutes with but moderate nausea. Small doses (gr.  $\frac{1}{30}$ ) given by the mouth are expectorant, and the same quantity, administered hypodermically, is said to have a hypnotic effect lasting from one to two hours. Large doses depress the heart and respiration, cause delirium and convulsions, and finally paralyze the motor and sensory nerves and the voluntary muscles. In a weak adult gr.  $\frac{1}{5}$  caused death by cardiac failure. Morphine kept for a long time in solution may become changed into apomorphine.

Codeine differs chemically from morphine in having the radicle methyl ( $\text{CH}_3$ ) replacing an atom of hydrogen, and may be considered a methyl-morphine. Like all methyl compounds it possesses motor-paralyzant power, like that of curare. On man it has some hypnotic action, but far less than that of morphine. It exalts the spinal cord more than morphine does, producing muscular tremor in excess of its sedative action. It has a special sedative influence on the pneumogastric nerve, contracts the pupils, and is remarkably analgesic to the nerves of the abdominal and pelvic viscera. When administered for several consecutive days it lessens the irritability of the digestive tract to such an extent that arsenic produces neither vomiting nor purging (Murrell). It markedly reduces the amount of sugar excreted by diabetics, but has no advantage over morphine in that respect.

Narcotine should be named Anarcotine, as it has little or no narcotic power. It is a convulsant in the lower animals and an antiperiodic in man.

Narceine is said by some observers to be remarkably hypnotic, and free from convulsant action; by others equally deserving of credit it is considered

almost inert. This alkaloid is difficult to obtain pure, hence the samples heretofore used have probably been contaminated with other alkaloids. It is said to possess laxative properties.

Thebaine is a powerful convulsant, exalting the spinal cord almost like strychnine and brucine. It is not used medicinally.

Cotarnine is closely related to Hydrastinine, both chemically and physiologically, being powerfully styptic and hemostatic by producing contraction of the arterioles.

Protopine and Cryptopine produce in frogs a condition of the voluntary muscles in which a series of electric shocks causes rapid clonic spasms instead of tetanic contractions. They also slow and weaken the heart, but accelerate the respiration.

The opium alkaloids, with the exception of protopine and cryptopine, in their action on the central nervous system form a series, in which Morphine stands at one end and Thebaine at the other. In this series the narcotic action is gradually replaced by reflex stimulation, the latter being most marked in the action of thebaine, which closely resembles that of strychnine. The most important members of the series may be arranged in the following order—morphine, papaverine, codeine, narcotine, thebaine,—the most narcotic being placed first and the most stimulant standing last.

#### Fatal Doses.

In a child one day old  $\text{ʒj}$  of Laudanum caused death. A medicinal dose given to a nursing mother proved fatal to the infant. A few drops of Paregoric have killed a child of nine months. In the adult gr.  $\frac{1}{2}$  of Morphine in one case, and gr. iv of crude Opium in another, have proved fatal.

#### THERAPEUTICS.

The chief indications for the use of Opium or Morphine are: to relieve pain from any cause except acute inflammation of the brain; to produce sleep, particularly in the insomnia of low fevers with delirium, in which a mixture of morphine and chloral is very efficient; to allay irritation in the various forms of acute nervous erethism; to check excessive secretion, as in diarrheas, dysentery, diabetes, and ptyalism; to support the system in low fevers and other adynamic conditions, when sufficient food cannot be retained; and as a sudorific, to produce sweating in coryza and other affections. It is a valuable remedy in irritative conditions of the stomach, bladder, or bronchi, also in severe vomiting, both forms of diabetes, gastralgia, colic and muscular spasm. In diabetes mellitus Morphine by the mouth reduces the sugar promptly, but when used hypodermically it has little or no effect thereon, even in the same case. In peritonitis and inflammation of other serous membranes, used freely even to narcotism it has often saved life. In cerebrospinal meningitis it is the chief remedy if given early, before exudation has set in. Cholera morbus and dysentery are often treated efficiently by a full dose of Opium, after emptying the bowel by castor oil or a saline cathartic.

In muscular rheumatism and acute colds Dover's powder as a diaphoretic, conjoined with hot drinks and foot-baths, is old but excellent treatment. In chronic mania and melancholia, nervous prostration and the delirium of fevers, Opium is one of the best hypnotics. In acute mania it does not act so well as Hyoscine, and in delirium tremens it should be used only in cases which show great prostration, and then for temporary effects alone, as a stimulant. In chronic melancholia small doses of Opium three times a day give better results than any other treatment. Severe pain from any cause (except cerebritis) is relieved by Opium with an efficiency possessed by no other drug, as the pain of sciatica, neuralgia, lumbago, cancer, renal and hepatic colic.

Cough of harassing and frequent character with but little secretion is best treated by Opium, but when there is profuse expectoration it should not be used, as the lowering of excitability of the respiratory centre which it produces would be dangerous in such a case. In nearly all acute inflammations it is valuable, especially when it becomes advisable to lock up the bowels. Its tranquilizing power over the circulation makes it invaluable in the various forms of hemorrhage, while in that from uterine fibroids and cancer the implanting of the opium-habit is deserving of consideration as a beneficial measure, as it checks and even stops the bleeding, as soon as established. Dyspnea from any cause is relieved by Morphine, especially that of cardiac disease; "it gives the power to breathe" (Huchard). In cardiac disease, especially aortic stenosis or insufficiency, with dyspnea, paroxysms of angina pectoris, or signs of cerebral anemia, Morphine hypodermically affords great temporary relief. Loomis used and recommended Morphine in full dose hypodermically for the uremic convulsions of *acute parenchymatous nephritis*, and this use of the drug has been endorsed by many clinicians and condemned by others of equal ability and experience. It is employed in puerperal convulsions with comparative safety when the nephritis is parenchymatous, but is highly dangerous in cases due to interstitial nephritis (Tyson). It is generally considered to be a dangerous agent in uremia, especially when due to chronic renal disease, either parenchymatous or interstitial.

Apomorphine as an emetic is of much service in poisoning, especially when swallowing is difficult, and it may be used with advantage in narcotic poisoning before narcosis has blunted the vagus centre. It is a valuable emetic in any case of poisoning where time is of great importance. As an expectorant it is one of the most efficient and useful agents at our command. In catarrh of the bronchi gr.  $\frac{1}{30}$  by the mouth every three or four hours is very beneficial, but the drug must be used in all cases with caution, especially in young children, who bear it very badly. In hacking coughs without expectoration it will prove serviceable, if given in very minute doses, not exceeding gr.  $\frac{1}{16}$  in the entire 24 hours. In phthisis it may be given in combination with morphine with advantage, especially in cases where there are dyspnea, continual and harassing cough, and thick, tenacious expectoration.

The two agents do not destroy each other's action, but from the combination we get increased secretion from the mucous membrane, with diminished irritability of the respiratory centre and consequently lessened cough (Brunton). In all conditions in which morphine is used to secure rest and sleep, better results will be obtained from gr.  $\frac{1}{2}$  with gr.  $\frac{1}{30}$  of apomorphine, than from larger doses of morphine given alone. In doses of gr.  $\frac{1}{30}$  hypodermically Apomorphine has proved efficient as a sedative in epilepsy, hystero-epilepsy, hiccough, spasmodic contractions and angina pectoris, and as a hypnotic in acute alcoholism; also in somewhat larger dose as a sedative and soporific in mental disease characterized by excitement with restlessness and a disposition to violence or suicide. It has been used successfully, by hypodermic injection, as an antidote to strychnine in dogs; and in one case, in which it was given in mistake for morphine, it entirely dissipated an acute and severe attack of sciatica. In small doses, gr.  $\frac{1}{30}$  hypodermically, it has been used as a hypnotic, and is said to produce a sleep lasting from one to two hours (Douglas).

Codeine is much employed as a palliative for cough, especially the irritable, hacking cough of phthisis unaccompanied by much expectoration. It seems to have a special influence on the nerves of the larynx, and will relieve a tickling night-cough better than any other opiate, if given in one dose of gr.  $\frac{1}{2}$  an hour before bed-time. In vomiting from almost any cause, doses of gr.  $\frac{1}{4}$ , repeated two or three times at hourly intervals, are usually very efficient. In the milder forms of diarrhea, gr.  $\frac{1}{2}$  to gr. j will generally check the disorder without inducing any unpleasant after-effects. In diabetes Codeine lessens the amount of sugar in the urine and often removes it entirely, but it must be given in large doses, beginning with gr. ij-iv, and rapidly increasing to gr. xv or xx. It is highly efficient in abdominal and pelvic pain, especially when ovarian in origin.

Cotarnine Hydrochloride is used internally as a hemostatic in hematemesis, pulmonary hemoptysis, and every form of uterine hemorrhage not due to fungus, neoplasms, or retained fragments of placenta; also locally in nasal and dental hemorrhage. Its sedative action is utilized in dysmenorrhea, and its contractile power on the uterine vessels is beneficial in subinvolution of the uterus. As it is not ecbotic it is available in the hemorrhage of threatened abortion.

#### *Applications of the Various Preparations.*

*Superficial pain* is often alleviated by the plaster or by extemporaneous liniments containing laudanum or some other fluid preparation. It is, however, very doubtful whether such applications are of direct value, as morphine is not absorbed by the unbroken integument; but the oleate is said to be very penetrating. *Intense pain*, as from the passage of calculi, is best met by the hypodermic injection of morphine sulphate in full doses (gr.  $\frac{1}{4}$ - $\frac{1}{2}$ ) with atropine sulphate (gr.  $\frac{1}{100}$ ). Either the solution of morphine or the

liquid preparations of opium may be given by the mouth in corresponding doses for the same purpose. Severe pain enables the system to resist the action of opium, which in such cases should be repeated at short intervals for effect, regardless of dosage.

*Sedative action* is obtained by different preparations for various organs. The stomach is best affected by the solution of morphine in effervescing mixtures, the extract in a small pill, or morphine given hypodermically over the epigastrium. The intestines may be influenced by laudanum in an enema of starch, or internally by Dover's powder, pulvis opii, or pil. opii, especially the latter with or without calomel, as an astringent when the bowel must be quieted, as in peritonitis, hernia, and intussusception. The rectum and other pelvic organs are promptly affected by a suppository of the extract of opium, gr.  $\frac{1}{4}$ , with gr.  $\frac{1}{12}$  of the extract of belladonna. The ovaries and the abdominal and pelvic organs generally are markedly susceptible to the analgesic action of codeine in doses of gr. j to gr. ij for an adult in severe pain.

To produce sleep the most efficient preparations are the tinctures, the solution of morphine, pil. opii and Dover's powder, in doses corresponding to the degree of insomnia and restlessness present.

Cough is relieved by the tinctures, and the solution of morphine in small doses with syrup of wild cherry or syrup of tolu; also by codeine in the last-named syrup. *Diaphoresis* is obtained by the use of Dover's powder in either of its forms.

#### Administration.

Probably no drug in the materia medica is so useful as Opium or has so wide a range of application. At the same time no other drug requires such careful handling, by reason of the many influences which modify its action and uses. Many persons are found with idiosyncrasies in respect to opium, some being easily narcotized, others being remarkably insusceptible to its action, and many suffer from a decided shock after its hypodermic administration, which may even produce alarming symptoms of collapse. In subjects of kidney disease it may accumulate and act more powerfully than expected, and generally it may be said to be *contraindicated* or to be used with great care in alcoholism, congestion of the brain, and advanced disease of the respiratory organs, heart and kidneys. Children bear Opium badly, and for them its proportionate dosage should be much below that for other agents. Morphine should not be given to children below 10 years of age, and never hypodermically to those beneath the age of 15. Opium given to a nursing mother will affect the child, being partly excreted in the milk.

The conjoint administration with opiates, of the spiritus ætheris, spiritus ætheris compositus, or spiritus ætheris nitrosi, an equal part with tinctura opii deodorati, will prevent the nausea often excited by the latter, and correct the drying-up effects of opium, due to its checking secretion. Some of its cerebral effects, as vertigo and mental confusion, are removed by a full

dose of potassium bromide, others are antagonized by quinine, and the general intra-cranial effects of the drug are to some extent opposed by digitalis and by tartar emetic.

Morphine and Atropine are sufficiently antagonistic to each other to make their combination extremely valuable as a therapeutic measure, and their use as mutual antidotes in poisoning by either a most efficient procedure if employed with due precautions, and intelligent consideration of their limitations (see the article on POISONING in Part III). When Morphine is given as a hypnotic or anodyne, Atropine should generally be administered at the same time in the proportion of gr.  $\frac{1}{120}$  of the latter to gr.  $\frac{1}{4}$  of the former. By this means the anodyne and hypnotic qualities of morphine are increased, while the nausea and depression with the subsequent dyspepsia and constipation due to it are avoided. Moreover, in the doses above mentioned atropine is a cardiac and respiratory stimulant, and will counteract the depressing tendency of morphine on the heart and respiration in subjects who are unduly susceptible to its action.

**OXYGENIUM, Oxygen, O.** This element is not official though it is extensively used in medicine. Its two combinations with Hydrogen, *Water*  $H_2O$ , and *Hydrogen Dioxide*  $H_2O_2$ , are official, also eleven other *Oxides*, namely—those of Arsenum, Calcium, Chromium, Ethyl, Iron, Lead, Magnesium, Manganese, Mercury, Silver and Zinc. It enters into the composition of most of the acids and their salts, many of the organic bases, and all the alkaloids except a few.

Oxygen is the most universally diffused element in nature, forming about one-fifth of the atmosphere, one-third of water, and a great part of the earth and the tissues of plants and animals. It is a colorless, odorless, and tasteless gas, of sp. gr. 1.1057, and can be liquefied by subjection to extreme cold and pressure combined. It was discovered by Priestley in 1774, and given its name, *Oxygen* (acid producer) by Lavoisier in 1778. It may be obtained pure from many of its combinations, but is usually prepared by heating Manganese Dioxide or Potassium Chlorate, or preferably both together. It is furnished by manufacturing chemists in all large cities, compressed in iron cylinders furnished with a rubber bag and mouth-piece by which to administer it.

**Ozone,  $O_3$  (Unofficial),**—is an allotropic form or condensed condition of Oxygen, three atoms of which are contained in a molecule of the former, instead of two as in the molecule of oxygen. Ozone exists in the atmosphere in the general proportion of 1 part in 10,000, but it is more abundant in the open country and on the ocean than in the air of cities. It is formed when an electric spark is passed through air, being then manifested by its peculiar odor. In the sick-room it may be produced by dissolving in water a mixture of manganese dioxide, potassium permanganate and oxalic acid.

#### Official Preparations.

**Aqua Hydrogenii Dioxidii, Solution of Hydrogen Dioxide, (Solution of Hydrogen Peroxide)** commercially known as Peroxide of Hydrogen,—consists of water to which nascent Oxygen has been presented, whereby an additional atom thereof has entered into combination with the hydrogen, producing  $H_2O_2$ . It is officially described as a slightly acid, aqueous