CANNABIS INDICA (Indian Hemp; Hashish).—This consists of the dried flowering tops of the pistillate or female plants of *Cannabis sativa*, an herb of the family Moraceæ, growing in India, Persia, southern Europe, America, and Africa. For a long time the strongly active hemp of India was believed a species distinct from the common hemp, and the name *Cannabis indica*, therefore, applied to it. It is now known, however, to be the identical plant, differing from ordinary hemp merely in the greater amount of pharmacologically active principle contained in it. The plant, indeed, attains its highest therapeutic power when grown in tropical or subtropical climates, inasmuch as it develops there a larger content of resin than elsewhere. Hemp imported from India is, however, by no means essential for good therapeutic results, Houghton and Hamilton having found (1908) samples grown in various localities of the United States and Mexico to be fully as active, clinically and experimentally, as the best imported hemp.

In the Orient the *churrus*, *charas*, or resinous exudation of cannabis is smoked and also introduced into an intoxicating drink. The Arabian *hasheesh* and Hindoo *bhang* are practically identical, being aromatic confections of which hemp forms the essential part. Another common way in which the drug is taken is in a sweetmeat of a green color, made with flour and various other ingredients.

The active constituent of cannabis is a reddish-brown oil or resin, generally termed *cannabinol*. According to Fränkel, the active substance is a phenolaldehyde the chemical formula of which may be expressed thus: $OH.C_{20}H_{28}COH$; cannabinol, however, appears to be merely a mixture of several resins and volatile oils, the exact nature of most of which has not as yet been determined. Wood, Spivey, and Easterfield described the entire resinoid exudation of Indian hemp as consisting of a terpene, a sesquiterpene, a paraffin, and cannabinol itself, of which they obtained 33 per cent. from one specimen of the "charas" and 16 per cent. from another. In common with other resins, cannabinol is insoluble in water, but dissolves in alcohol, ether, chloroform, and oils. Choline is also known to be a constituent of cannabis; likewise is, possibly, the crystal-

line substance *cannabine*, which is considered to be an alkaloid. Other alleged components of cannabis probably represent simply modifications of the mixture "cannabinol" arising through different methods of isolation. The whole subject of the chemical constitution of cannabis is still in a state of uncertainty and confusion. According to Lees, watery extracts of the drug contain some active ingredient.

PREPARATIONS AND DOSE.—Following are the official preparations of cannabis, in addition to the crude drug, the dose of which is 1 grain (0.06 Gm.):—

Extractum cannabis indicæ (extract of cannabis indica). Dose, ⅕ to 1 grain (0.012 to 0.06 Gm.).

Fluidextractum cannabis indicæ (fluidextract of cannabis indica). Dose, 1 to 5 minims (0.06 to 0.3 c.c.).

Tinctura cannabis indicæ (tincture of cannabis indica), 10 per cent. Dose, 15 to 30 minims (1 to 2 c.c.).

The first-named quantity under each of these preparations is the official dose. Since hemp preparations are very subject to deterioration, however, the larger dose mentioned will not infrequently have to be attained before the desired therapeutic effects appear.

Some of the unofficial preparations containing or derived from cannabis indica are as follows:—

Mistura chloroformi et cannabis indicæ composita, N. F. ("chloroform anodyne"), 1 fluidram (4 c.c.) of which contains approximately 7½ minims (0.5 c.c.) of chloroform, 11 minims (0.75 c.c.) of tincture of cannabis indica, ⅐ grain (0.009 Gm.) of morphine sulphate, and 2 minims (0.12 c.c.) of tincture of capsicum. Dose, ½ fluidram (2 c.c.).

Mistura chlorali et potassii bromidi composita (chloral and bromide compound), 1 fluidram (4 c.c.) of which contains about 12 grains (0.8 Gm.) each of hydrated chloral and potassium bromide, and ⅛ grain (0.008 Gm.) each of the extracts of cannabis indica and hyoscyamus. Dose, fluidram (4 c.c.).

Pilula antineuralgica (Brown-Séquard), containing the extracts of hyoscyamus, conium, ignatia, opium, aconite, stramonium, and belladonna, with ¼ grain (0.016 Gm.) of extract of cannabis indica. Dose, 1 pill.

Collodium salicylatum compositum (corn collodion), consisting of salicylic acid, 11 parts, and extract of cannabis indica, 2 parts, in flexible collodion, enough to make 100 parts. Used locally.

Cannabine, a dark-brown, viscid mass, with the odor of hemp, soluble in alcohol and ether; believed to be an alkaloid. Dose, 1 to 4 grains (0.06 to 0.25 Gm.).

Cannabine tannate, a yellowish-brown powder, having a strongly astringent, somewhat bitter taste. It is very slightly soluble in pure water or alcohol, but dissolves more readily in these fluids when an alkali has been added to them. Dose, 4 to 15 grains (0.25 to 1 Gm.).

Cannabinon, a preparation of the resinous mixture cannabinol, having a disagreeable taste. Dose, ½ to 1 grain (0.03 to 0.06 Gm.)

Cannabindon, a dark, cherry-red syrup, with an unpleasant taste and insoluble in water. Dose, ½ to 1 minim (0.03 to 0.06 c.c.).

Cannabinine, a brownish, syrupy liquid with an odor similar to that of

nicotine. Dose, ¼ to 1 minim (0.015 to 0.06 c.c.).

These preparations, though claimed to be superior to the official ones in that a closer approximation is made to the true active constituent of the drug, appear to deteriorate with the same readiness, and do not offer any marked advantage over the galenical drugs. Chemical methods of assaying cannabis products not being practicable because of the prevailing uncertainty concerning the nature and number of the contained active substances, a biological procedure for standardization, consisting in the injection of the drug in dogs and observation of the amount of drug required to cause a given degree of inco-ordination, has been generally adopted, which gives reliable, though only approximate results. The physician prescribing cannabis should by preference use recently standardized products, as preparations kept for any length of time are likely to have undergone considerable deterioration. It is said that, in India, dealers in the drug refuse to buy the old crops of cannabis after the new ones are gathered, and that after two years the crops are publicly burned.

> Determination of the physiological activity of *Cannabis sativa* by internal administration to specially selected dogs is reliable when the standard dose, 0.01 gram per kilo of body weight, of the unknown, reduced to a solid extract, is tested on the same animals in comparison with the same quantity of a standard U. S. P. extract by an experienced observer. Houghton and Hamilton (Therap. Gaz., Jan., 1908).

MODES OF ADMINISTRATION.—The preparations of hemp are active only when given by mouth or rectum. When administered subcutaneously the resin remains unabsorbed, no effect being, therefore, produced. The fluidextract or tincture of the drug may be given either in an alcoholic flavored preparation (with a little chloroform—Goodwin), on a piece of moist sugar (washed down with water), or in a small quantity of wine. The extract is employed where the remedy is to be given in pill form. Where no standardized preparation is available, the initial dose should be small, as some specimens prove unexpectedly powerful.

Goodwin advises that, as a rule, cannabis indica be not given to a patient unless the latter has confidence in the physician, and that in giving any but the smallest doses the patient should be forewarned that some peculiar symptoms might arise, though also assured that there would not be the slightest danger.

INCOMPATIBILITIES. — Addition of even small amounts of water to alcoholic preparations precipitates the active resin cannabinol. Acids, strong alkalies, and strychnine are also incompatible.

PHYSIOLOGICAL ACTION.—Nervous System.—The action of hemp on the brain consists of a combination of depression with stimulation, the latter being most marked in the initial stage of the effects and when large doses are used. Like opium, cannabis tends to plunge the patient into a condition of semiconsciousness, with loss of the power of judgment, but great activity of the imagination. Continuity of thought becomes impossible, and the subject, impelled at first to unusual physical activity, associated with a feeling of unwonted well-being, may execute

various senseless acts, talk at random, and exhibit merriment to an absurd degree. Especially characteristic is a loss of the power of appreciating distance and time, near objects generally seeming remote and minutes lengthened to hours. With small doses, these evidences of primary stimulation are frequently absent or but slightly marked—especially in European races, in contradistinction to Orientals—and the drug acts chiefly as a hypnotic and analgesic. After a period of drowsiness the patient passes into a quiet sleep, from which he finally awakes, after a variable interval, without experiencing any unpleasant after-sensations of languor, nausea, or headache.

In addition to its effects on the intellectual functions, cannabis indica exerts a distinct action of peripheral sensation. The pain sense is obtunded or abolished and the tactile sense rendered less acute. More or less pronounced numbness and tingling may precede these effects. That the motor portions of the nervous system may also be influenced is shown by the increased movement and even convulsions sometimes observed after large doses, as well as the inco-ordination seen in dogs to which the drug has been administered for purposes of standardization. In frogs, sensation is lost before the power of voluntary movement.

According to Dixon, the effects of hemp vary with the mode of its introduction into the system. Exhilaration is most manifest when the drug is smoked; where it is taken by the mouth in small amounts exhilaration does not generally occur. Dixon states that inhalation of the drug will remove the sensations of muscular fatigue which follow hard physical labor, and act as a cerebral stimulant.

Circulation. — Ordinary doses of cannabis indica, taken internally, produce little, if any, change in the circulatory functions, though inhalation of the drug is capable of accelerating the heart action. Large doses tend likewise to increase the cardiac rate, probably in part owing to the increased motor activity induced. Poisonous amounts have been shown by Dixon to cause death by circulatory rather than respiratory failure.

Alimentary Tract.—Unlike most opiates, cannabis does not disturb digestion and bring on constipation. It appears often to increase the appetite; the reason for this is not as yet definitely known.

Kidneys.—Cannabis has been credited with possessing a diuretic effect, though this is probably never very marked. According to Dixon, fresh hemp is diuretic, while the dried plant exerts but little such action.

Other Effects.—The drug tends to dilate the pupils. It sometimes acts as an aphrodisiac, and has been stated to stimulate the uterine contractions where there is inertia. Locally, it is believed to possess slight analgesic properties.

ABSORPTION AND ELIMINATION.—Cannabis indica is absorbed slowly from the gastrointestinal tract, one or two hours elapsing before its effects appear. It is not absorbed when given subcutaneously. Elimination of the drug is likewise slow; after full doses the effects may persist twenty-four or thirty-six hours. The chief channel of elimination appears to be the urinary tract.

POISONING BY CANNABIS INDICA.—Large single doses of

Indian hemp induce to an exaggerated degree the mental disturbances already noted under Physiological Action. Marked exhilaration, inordinate laughter or singing, great restlessness, and accelerated heart action are characteristic of the earlier stage of its action. These are followed by numbness of the limbs, anesthesia of the skin, inco-ordination, not infrequently a fear of impending death, sometimes more or less marked convulsive phenomena, and then profound sleep or coma. Bicknell reported a case in which there was a sensation as of extreme tension in the abdominal blood-vessels, which felt distended almost to bursting. After extremely large doses depression of the circulation and respiration may appear, but death from cannabis indica poisoning is, to say the least, very rare, no case terminating fatally from this cause having apparently been recorded. Houghton and Hamilton injected 2 ounces of the U. S. P. fluidextract into the jugular vein of a dog; after being unconscious about a day and a half, the animal recovered completely.

Cases reported of 2 brothers, aged 20 and 22, each of whom took 90 minims (5.55 c.c.) of tincture of cannabis indica. Different effects were produced in the two cases: In the younger, the beginning of the period of excitement was delayed for some little time and its onset was gradual. The effect of the drug wore off slowly, the pupils remaining dilated for four days. There was a fresh outburst of excitement twenty-four hours after the taking of the drug, following an apparently normal period of ten hours. In the elder brother the onset was almost instantaneous, excitement reaching a climax at once. Later this gave way to extreme mental depression and numbing of sensation. In only 1 case was sleep accompanied by dreams. In neither case did the drug produce its reputed aphrodisiac action. James Foulis (Edinburgh Med. Jour., Sept., 1900).

Treatment of Poisoning.—Tannic acid and an emetic may be given to remove from the body whatever portion of the poison is still unabsorbed. The administration of lemon juice has been recommended. If circulatory or respiratory depression should happen to appear, stimulants such as caffeine, digitalis, and strychnine may be given, external heat applied, and artificial respiration practised if necessary.

Chronic Poisoning, or "Hashish Habit."—This is observed almost exclusively in eastern countries, where hashish is employed in the form of a beverage for purposes of intoxication. Persistent overuse produces a condition of general functional incapacity characterized by reduction or loss of the will power and ability to concentrate the attention, stupor and physical weakness, tremor, anorexia, pallor, yellowness of the eyeballs, diminished peripheral sensation, and loss of sexual power. If the abuse be further continued, insanity, in the form of chronic mania or melancholia, supervenes. In some cases a form of delirium analogous to delirium tremens, and accompanied by terrifying hallucinations and a tendency to destructiveness, is seen. The nutrition of the body appears to be, in general, less seriously affected by chronic hashish abuse than in opiumism, possibly because there is less interference with the digestive functions.

The moderate use of hemp drugs is practically attended by no evil physical effects. Excessive use, however,

does cause injury, tending to weaken the constitution and render the consumer more susceptible to disease, possibly dysentery and bronchitis. Moderate use produces no injurious effects on the mind, except in cases of marked neurotic diathesis. Excessive use both indicates and intensifies mental instability. It tends to weaken the mind, and may even lead to insanity, especially in cases where there is already weakness or hereditary predisposition. Report of Indian Hemp Drugs Commission (Therap. Gaz., April, 1905).

There is no proof that cannabis-indica extract by itself, taken internally or even smoked, causes a habit, and to continue to list it with such habit-forming drugs as morphine, chloral, and alcohol greatly detracts from whatever value it might possess as a sedative. M. V. Ball (Therap. Gaz., Nov., 1910).

THERAPEUTICS.—As a Sedative or Hypnotic.—In **insomnia** due to nervous exhaustion, Indian hemp is a useful, though somewhat uncertain, remedy. In **senile insomnia,** with a tendency to wandering and temporary mental aberration, the use of the drug in moderate doses has been highly lauded by Reynolds; likewise, in the occasional nocturnal restlessness of paretics. While its effect cannot be relied upon to the same extent as that of opium, it possesses over the latter drug the advantages of not disturbing the gastrointestinal functions and of not causing headache, nausea, or lassitude, and may therefore in a certain proportion of cases prove preferable to it.

One of the chief uses of cannabis indica for somnifacient purposes is in certain forms of insanity, viz., **melancholia** and **mania.** In the former it has, in addition, been credited with the power of converting mental depression into exaltation. In **delirium tremens** the drug has also been used with some degree of success. It tends to dissipate the horrors and overcome the nervous hyperesthesia. In **chorea** the use of cannabis has been recommended by Suckling. In **tetanus** and **rabies** good results have also been reported.

Cannabis indica used in **delirium tremens** for forty years without the loss of a single case. In alcoholic mania the drug also proved satisfactory. E. B. Silvers (Med. Bull., April, 1907).

In the form of vasomotor coryza popularly denominated **"hay fever"** or "hay asthma," the employment of cannabis indica has been suggested, for the purpose of allaying the excessive irritability of the nervous system.

In **bronchitis, pulmonary tuberculosis,** and other forms of respiratory disease associated with throat irritation and cough, cannabis indica may be used with advantage as one of the ingredients of a cough mixture. According to Lees, it occupied a place in this connection which cannot be filled by any other drug, as it tends both to alleviate the paroxysms of coughing and exert a stimulating effect. It relieves tickling sensations in the throat and is superior to opium in that no digestive disturbance or other unpleasant side-effect is produced.

Other affections in which the sedative properties of this drug have been utilized include **paralysis agitans, exophthalmic goiter, spasm of the bladder,** whether of nervous or inflammatory origin, and **gonorrhea,** in which the symptom **chordee** may be relieved by it. It is also said to reduce the amount of pus formed in the last-named disease.

As an Analgesic.—Cannabis indica has come into widespread use as a remedy for pain of various kinds, more especially in the **headaches** attending migraine, eye-strain, the menopause, and even brain tumors or uremia. In true **migraine** it was formerly used extensively in combination with gelsemium for the purpose of arresting the attacks. It may also be used alone in a full dose to abort a paroxysm, or in small doses three times daily for some weeks to prolong the intervals between attacks (Goodwin). In "sick headaches" Murrell advises that the extract of cannabis be administered in doses of from ⅛ to ½ grain (0.008 to 0.03 Gm.) in pill form. When the patient is suffering constantly from headache, or is liable to an attack on the slightest provocation, such a pill may be taken three times a day for weeks at a time without fear of the production of any untoward effect.

It is especially in pain due to direct involvement of the nerves, rather than in pain associated with inflammatory conditions in general, that cannabis is effective as an analgesic. In **tic douloureux** and other **neuralgias,** the drug has often been found efficient. In **gastric ulcer** Suckling has seen it increase the efficacy of silver nitrate when given in combination with it. In **gastralgia** a pill combining cannabis with bismuth may be used.

Reynolds employed the drug with success in the lightning pains of **tabes,** and it has also been recommended in **multiple neuritis.** In certain malarial states associated with severe headache and nervous symptoms, cannabis is said to be a useful adjuvant to quinine.

Cannabis indica is an invaluable remedy in the treatment of disturbances of the sensory centers. It is one of the best remedies in **headaches** of many kinds, and is especially useful in cephalic sensations so common in individuals of neurotic habit. Tincture or fluidextract preferred; 5 to 10 drops (0.3 to 0.6 minim) of fluidextract may be taken on moist sugar, swallowed with a draught of water. Angel Money (Austral. Med. Gaz., Feb., 1900).

With a few exceptions, the efficacy of cannabis indica is limited to those diseases directly traceable to nervous derangement. **Pain** not due to distinct pathological lesions forms the chief indication for its administration, and relief is usually obtained promptly. H. W. Lewis (Merck's Archives, July, 1900).

In various uterine disturbances associated with pain, as **nervous** and **spasmodic dysmenorrhea, subinvolution,** and chronic inflammatory states, cannabis indica appears to exert a distinctly useful effect. Not only is pain relieved, but hemorrhage, where present, diminished or arrested. Therefore in **menorrhagia** and impending **abortion** the drug may also prove useful. It is said to be efficacious as a preventive of **postpartum hemorrhage,** but requires to be given in full doses and, with advantage, in conjunction with ergot. For chronic ovarian hypersensitiveness, cannabis indica may also be used with benefit.

Following suppository recommended for **dysmenorrhea**:—

℞ *Ext. cannabis indicæ,*
Ext. belladonnæ foliorum .....āā gr. ¼ (0.015 Gm.).
Olei theobromatis ..... q. s.

Ft. suppos. no. j. Da tales no. xx.

Sig.: Introduce one every evening, commencing with the fifth day before the menses. V. Robinson (from Jour. de méd. de Paris; Med. Rev. of Rev., March, 1912).

In **acute articular rheumatism** the analgesic property of cannabis has also occasionally been utilized.

In skin affections associated with intense itching, such as **eczema** and **senile pruritus,** the internal administration of Indian hemp will often give relief where local applications fail. It is best, perhaps, to give it in small doses at first and gradually increase (Mackenzie). According to Reynolds, the drug will relieve tingling, formication, and numbness in **gouty** subjects.

According to Aaronsin, cannabis indica may be employed locally with good effect for the relief of **dental pain.** The tincture is diluted with 3 to 5 parts of alcohol and introduced into the cavity of the tooth by means of a tampon of cotton. Such a tampon may also be placed about the gums below the tooth. If the alcohol proves irritating the preparation should be diluted with hot water. It must be stated that Aaronsin's recommendation constitutes only an isolated observation in favor of the use of cannabis as a local anesthetic, which appears to be discountenanced by other authors owing to a supposed primary irritating action of the drug which precedes the local anesthetic effect.

Other Uses.—In certain disorders the use of this drug was recommended by Germain Sée. Thus, in **gastric neuroses** and **dyspepsia,** respectively, it tends to allay pain and improve the appetite. In the presence of **hyperchlorhydria,** according to the author mentioned, it acts as a sedative and improves digestion. Alkalies and purgatives should be used in conjunction with it. In the pronounced **anorexia** following exhausting diseases, from 5 to 10 minims of the tincture of cannabis **indica,** or ¼ to ½ grain (0.015 to 0.03 Gm.) of the solid extract given three times daily before meals, will often cause a return of the appetite in two or three days (McConnell). The drug is superior to opium for use in most gastric disturbances in that it does not tend to constipate.

For **pulmonary tuberculosis,** when accompanied by insomnia and dyspepsia:—

℞ *Strychninæ sulphatis* ... gr. 2/3 (0.043 Gm.).
Ext. opii .... gr. j (0.065 Gm.).
Ext. cannabis indicæ ..... gr. iss (0.1 Gm.).
Phenylis salicylatis .... gr. c (6.5 Gm.).
Aloini ..... gr. ss (0.032 Gm.).

M. et pone in capsulæ no. xx.

S. G. Bonney (Med. Rev. of Rev., March, 1912).

In **intestinal indigestion,** with diarrhea, and in dysentery, the drug may also be of great service, tending to diminish local irritability and excessive peristalsis. In the Orient, cannabis has long been a favorite remedy for **Asiatic cholera.** Here it appears to act, however, rather through temporary stimulation of the nerve centers, tending to revive the patients from collapse, than upon the intestinal condition. According to Marshall, the beneficial influence of cannabis in **menorrhagia** and **dysentery** is due not to the active substance, cannabinol, but to the terpenes it also contains.

In **nephritis, acute** or **chronic,** can-

nabis indica has been stated to overcome **hematuria** and pain, when these symptoms are present.

In **diabetes mellitus** cannabis indica, used continuously, will often cause a marked improvement in all the symptoms, without checking the secretions or causing constipation, as would opium.

In **cardiac palpitation,** as well as in some cases associated with **vertigo,** cannabis indica has been used with asserted good results (Sée).

The efficiency of the drug as an **aphrodisiac** appears, at least in western races, to have been overestimated. In moderate doses the effect of the drug is said to be rather a sedative one. In case of hyperirritability of the genital mechanism in the male, with resulting functional impotence due to premature discharge, cannabis indica, by diminishing peripheral sensibility, tends to promote normal completion of the procreative act (Goodwin).

In the treatment of **sexual atony** in the female the following combination has been recommended:—

℞ *Extracti cannabis indicæ,*
Extracti nucis vomicæ .....āā gr. xxx (2 Gm.).
Extracti aloes .... gr. vij (0.5 Gm.).
Ft. in pil. no. c.
Sig.: One pill three times a day.

For **impotence:**—

℞ *Ext. cannabis indicæ,*
Ext. nucis vomicæ ..āā gr. xv (1 Gm.).
Ext. ergotæ (aqu.) ..... ʒj (4 Gm.).
Ft. in pil. no. xxx.
Sig.: One pill morning and evening.

Da Costa (quoted by V. Robinson, Med. Rev. of Rev., March, 1912).

Cannabis indica is a constituent of many preparations employed externally in the treatment of **corns,** including the Collodium salicylatum compositum of the National Formulary. In **ichthyosis hystrix** Van Harlingen applies the following preparation:—

℞ *Acidi salicylici* ..... ʒss.
Ext. cannabis indicæ .. gr. x.
Collodii ..... fʒj—M.

C. E. de M. Sajous
and
L. T. de M. Sajous,
Philadelphia.