the fixed oils. The crystals contain 78.39 parts of iodine and melt at 121.5° C. (250.5° F*).
Unlike jodoform, losophan does not yield free jodine on

contact with the animal tissues, and so cannot truly substitute iodoform in medical practice. It has been used as a local antiseptic, but with questionable advantage. It may be applied in a one- or two-per-cent. solution in alcohol and water (alcohol three parts, water one part), or in an ointment of from one- to ten-per-cent. strength, with basis of vaseline or a mixture of vaseline one part, and lanolin four parts

Losophan is not official.

phen, tetraiodophenolphthalein, (CeH2I2.OH)2 C<C₆H₄CO. This compound, behaving as an acid,

occurs as an impalpable, pale yellowish powder, odorless and tasteless, insoluble in water and difficultly so in alcohol, ether, and chloroform, but soluble in alkalies, with which substances it combines to form salts. Nosophen contains 61.7 per cent. of iodine.

Like losophan, nosophen does not yield iodine on contact with the animal tissues. It has been used, however, for the purposes of iodoform, and is unirritating and non-poisonous. It may be applied freely in its powder

The sodium salt of nosophen has been used in medicine under the name of antinosine. This salt occurs as a dark blue amorphous powder, and is freely soluble in both water and alcohol. It may be used for local antiseptic purposes in solutions varying in strength from one to three per cent., which solutions are without odor or taste.

The bismuth salt also has been used under the name of eudoxine. This substance is a reddish-yellow powder, tasteless and odorless, and insoluble in water. It is decomposed by alkalies with the formation of antinosine It has been given internally, for gastro-intestinal derangements, in doses of from 0.03 to 0.50 gm, (gr. ss.-viii.) and is assumed to undergo conversion into antinosine by the action of the alkalies in the intestinal fluids.

Nosophen is not official.

For europhen, see article under its own title. Edward Curtis

IODOFORM. (TOXICOLOGICAL.)-In 1880 Mosetig von Moorhof introduced iodoform as a surgical dressing. Since that time it has been largely used by surgeons not only as a dressing, but also (in solution) for injection into chronic abscesses, tuberculous joints, etc. In many cases grave symptoms have supervened; sometimes followed by recovery, occasionally by death. Such cases have been steadily reported since 1882, but now there seems to be a lull, probably owing to the fact that iodoform is not in such general use as formerly

Cases have been reported of which we may mention: (1) A series of four, all of which ended in recovery, described by Marcus Beck, of London (Brit. Med. Journal, 1882, i., p. 903). (2) Barois (Archiv. de Méd. et de Pharm. Milit., 1890) has collected a series of forty-two fatal cases, and adds one of his own; the remarkable point in this series is that there is only one case of an American surgeon, viz., that of Dr. Sands, in 1881, in which about one and a half drachms were used in dressing after colotomy for cancer of the rectum. (3) Andry's series of four (Lyon Médical, 1890), one of which proved fatal. (4) Gerlach's series of four cases, all of which terminated in recovery (Medical News, Philadelphia, 1891, p. 273).

Iodoform is generally applied either (1) pure, as a powder, (2) combined with collodion, (3) dissolved in ether, (4) incorporated with gauze, or (5) as an emulsion in gly Of these the iodoform gauze is probably the safest. An alkali added to the iodoform is said to render it less toxic When iodoform is used mercurials and carbolic acid should be avoided. Iodoform is quickly absorbed and slowly eliminated; clean, granulating wounds, large surfaces, fatty tissues, burns, sinuses, fis tule and abscess cavities are particularly favorable for the absorption of iodoform.

Toxic Dose.—The smallest dose known to have pro-

duced toxic symptoms is less than one grain. This was a case reported by Dr. Tiffany, of Kansas City (St. Louis Med. and Surg. Journ., xxxviii., 562), in which a fraction of a grain of iodoform was applied to the tympanum through the external auditory meatus. The patient, a woman, who had an idiosyncrasy to the drug, suffered from inflammation, swelling, and erysipelas; recovery followed on withdrawal of the drug. The smallest *fatal* dose is probably about forty-five grains. The case, which is reported by Barois (see above), was one of large cold abscess under the left pectoralis major; an injection of about fifty-five grams of a five-per-cent, ethereal solution was used; symptoms of ether narcosis immediately followed, then symptoms of iodoform poisoning, chiefly cerebral, and death in coma after nine days. Fatal results from doses of one drachm and upward have been reported But, on the other hand, a case has been recorded in which a woman took two drachms of iodoform at a single dose. with no worse result than severe headache, griping pains in the abdomen, and purging; but the odor and taste of the drug remained for several days.

It must be borne in mind (1) that many toxic effects may have been due to impurities in the drug; (2) that some people are particularly susceptible to iodoform. and many cases of iodoform poisoning are due to idiosyncrasy; (3) that iodoform seems particularly dangerous in wounds and injuries of the breast, axillary space, and chest wall, and therefore great care should be taken in

using the drug in these regions. SYMPTOMS.—The cause of the toxic symptoms is the iodine. Iodoform (CHI_s), which contains more than ninety-six and one-half per cent. of iodine, is decomposed by the tissues with which it comes in contact, and iodine is liberated. This free iodine promptly combines with the albumin of the tissues, and the result is an unstable albuminate of iodine, which passes into the circulation and thence to the various organs of the body.

Schede, of Hamburg, describes six classes of cases of poisoning by iodoform: "(1) High fever without other phenomena. (2) Fever, with mild gastro-intestinal irritation, depression of spirits, and rapid pulse; recovery almost invariable. (3) Very rapid, soft pulse, from 150 to 180; no fever; great danger. (4) Very rapid pulse with high fever; death almost invariable. (5) After severe operations, rapid collapse and death. (6) A form resembling meningitis, somnolence followed by stupor; contracted, motionless pupils; restlessness, temperature normal, and pulse exceedingly rapid; most characteristic and severe" (from H. C. Wood's "Therapeutics").

We prefer a simpler classification: 1. Local or cutaneous or eruptive. 2. General or constitutional: (a) with

cerebral symptoms; (b) with coma.

1. Local, Cutaneous, or Eruptive.—This is the commonest form and generally follows the application of iodoform as a dressing. There is a dermatitis of an crythematous type, or an eczematous eruption. The part is swollen and is covered by many small thick-walled vesicles. These vesicles become confluent and are filled with a serous fluid which may later become tinged with blood. The epidermis is at first raised; later it peels off, and leaves an exposed area of very sensitive corium bathed in a serous exudate

2. General or Constitutional (a) with Cerebral Symptoms. —This may occur some time after the application or injection of the iodoform, or almost immediately. The symptoms are the odor of iodoform in the breath; yellow liscoloration of the skin and conjunctivæ; increase of temperature; pulse small, irregular, and rapid (up to 160 or 180); faintness, vertigo, severe headache, thirst, nausea, vomiting, gastro-intestinal irritation, muscular twitchings; the patient becomes melancholic and has delusions of persecution and possibly suicidal tendencies. hence must be carefully watched; there is maniacal excitement, which may subside on removal of the dressing. 'There is nothing specific in iodoform mania; it may occur with the first dressing, or it may result from its prolonged use; it gives rise to restlessness, to sleeplessness, to irritability passing into mania, and the mania

may rapidly give place to stupor or mental weakness" (Dr. Savage, in Allbutt's "System of Medicine," vol. viii., 315). Barois found in severe cases that the symptoms came on suddenly and early; first mental depression, then excitement.

(b) With Coma.—This is the most severe form. The pulse is rapid and feeble; there is rigidity of the neck, as n meningitis; great mental confusion with misplacing of words; there may be paralysis of the sphincters; the patient becomes emaciated, lethargic, and falls into a state of coma and dies

Death occurs from paralysis of the heart. Age increases the susceptibility of most persons to the action of the drug. Tuberculous and cachectic patients are said to give worse results than others; but probably iodoform is more often administered to these patients than to others

Pathology.—The post-mortem findings are fatty degeneration of the heart, liver, kidneys, and muscles; hyperæmia of the meninges and some atheromatous lesions of the arteries. Barois found occasionally a partial infiltration of the lungs, with degeneration of the alveolar epi-

Prognosis.—This is bad. It probably depends upon

idiosyncrasy as well as dose.
Prophylaxis.—Get a pure preparation of the drug; use as small an amount as possible; remember idiosyn-erasy; be particularly cautious in wounds of the breast, chest walls, and axillary space.

TREATMENT. - In every case stop the application of further iodoform; then keep up the patient's strength and remove as much as possible of the drug with water, a warm solution of starch, oil of eucalyptus, or ether and cotton; and give diuretics, diaphoretics, and a hot bath to hasten elimination. In a case reported by Dreesmann of Bonn (Beitr. zur klin. Chir., v., 9, p. 233), hypodermic injections of twenty-per-cent. solution of iodoform oil were repeatedly given for white swelling of the knee; neurotic symptoms followed, and on resection of the knee a mass of iodoform the size of a cherry was found just above the condyles; the neurosis ceased on the removal of this. Apply dressings of decinormal salt solution, snip off the top of any vesicles that may be present, so that the solution may reach the corium underneath; locally apply some non-irritating alkaline fluid to neutralize the nascent iodine, and thus prevent its entering into combination with the albumins. Give stimulants, and to increase the alkalinity of the blood administer potassium acetate, po-tassium bicarbonate, or potassium bromide; this latter is recommended, and may be administered in an initial dose of gr. xv. in \(\frac{7}{2} \) ij. of water, followed by gr. x. every hour.

\[\begin{align*} R. J. E. Scott. \]

10DOGALLICIN is an iodine compound of gallicin (see Gallicia), and is a gray amorphous powder which is insoluble in all ordinary media. It contains 38 per cent. of bismuth and 23.6 per cent. of iodine. It is antiseptic. locally anæsthetic, and desiccating, and may be applied in powder or in five-per-cent. lanolin ointment for wounds, ulcers, trachoma, and corneal ulcers. W. A. Bastedo.

10D0L. - Tetra-iodo-pyrrol, C4I4NH. This compound of iodine may be prepared by dissolving pyrrol in alkaline water and mixing it with a solution of iodine in iodide of potassium. The precipitate is collected, dissolved in alcohol, and reprecipitated. It is also obtained by the reaction that takes place when alcoholic solutions of pyrrol and iodine are mixed for twenty-four hours. Iodol separates when the mixture is added to water.

It is a pale yellow, finely crystalline powder. It is without taste and does not possess any disagreeable odor. It is insoluble in water, and very slightly soluble in dilute alcohol. Strong alcohol dissolves one part in six; glycerin, one part in thirty-four. Iodol is very soluble in ether and chloroform. It contains about ninety per cent. of iodine. Heated to 140° or 150° C. it is decomposed with the evolution of violet iodine vapors.

Iodol was introduced in 1885 by Ciamician and Silber,

as a substitute for iodoform, its freedom from any disa-greeable odor being a decided advantage. Like iodoform it does not rank high as a germicide, but it has the same power of inhibiting the growth of bacteria and maintainag a surface clean and aseptic. To wounds, ulcers, and Il suppurating surfaces it is applied in the same manner as iodoform, by dusting the powder on the part or making it into an ointment with lanolin or vaselin. It may also be used in solution of alcohol, ether or collodion. Ether 5 parts, collodion 50 parts, iodol 1 part is a favorite combination for local application. For gynæcological purposes a solution of iodol, spirits, and glycerin, 1 to 16-34, may be used for saturating tampons, etc. Its local use has been highly recommended for ulcerations of the nose, pharynx, and larynx, particularly when due to a tuberculous or syphilitic cause.

Iodol has been employed internally with success in conditions of the stomach and intestines accompanied by putrefactive and fermentative changes. It has been used with success in gastro-intestinal catarrh and ulceration of the mucous membrane. When its action is directed to the stomach it should be given in the intervals between meals; when it is desired to act on the intestinal canal, the most favorable time for its administration is immediately at the close of the digestive process. As its constituent at the close of the digestive process. As its constituent iodine is excreted in part by the rulmonary organs, it has been used in bronchitis, phthisis, and various diseases of this locality. In these conditions, in addition to its internal administration, inhalations and insufflations have been used. In syphilis it is also recommended, especially in tertiary forms of the disease in which it has given the best results. It is well borne by the system, having no effect on the temperature, circulation, or respiration; iodism is of very rare occurrence. It is also thought to be of benefit in diabetes. The dose is from one to three grains, two or three times a day; it should be given in wafers or pill form.

10D0MUTH (Bi₄C₇H₇I₂O₅) is a bismuth iodine compound, used as a dusting powder for wounds, ulcers, etc. It has been given internally as an alterative in dose of gm. 0.06-0.6 (gr. $\frac{1}{10}$ -i.).

IODONAFTAN is a naphtha ointment base containing three per cent. of iodine. It is a very smooth, stable ointment of pleasant odor. It is blackish-brown in color, ointment of pleasant odor. It is blacking appearing dark green by transmitted light.

W. A. Bastedo.

10D0NAPHTOL - BETA. — Naphtol-beta di-iodide. Also termed Naphtol-aristol. This derivative of iodine was introduced by Dr. Braille (Répert. de Phar., November 10th, 1891) as a substitute for iodoform, aristol, and other iodine compounds. It is prepared by mixing a solution containing 24 gm. of iodine and 27 gm. of potassium iodide with another solution containing 110 gm. of naphtol-beta and 40 gm. of caustic soda. There is then added a little solution of the hypochlorite of sodium cor-responding to ten times its volume of chlorine. Iodonaphtol is then precipitated. It is a greenish-yellow powder, inodorous, tasteless, insoluble in water, very slightly soluble in alcohol, but soluble in ether and chlo-

It is recommended for the treatment of wounds, ulcers, and all conditions in which iodoform and other antiseptics are employed. It is applied as a powder dusted on the part affected.

IODOPHENIN .- Iodophenacetin. This compound of iodine and phenacetin was described by Dr. Scholvein, in 1891, at a meeting of the Berlin Pharmaceutical Society. It contains fifty per cent. of iodine and forms in steel-blue crystals, with an odor of iodine, and a burning taste; it colors the skin yellow. It is insoluble in water, solu-ble in alcohol and glacial acetic acid. Heated, or even when mixed with water, it is decomposed and iodine is

It is recommended as a useful antiseptic, and experi-

ments show that it possesses this property in a marked degree, but it also has the irritating effects of free iodine.

When employed as an internal remedy it forms combinations with the alkalies of the intestinal canal, and, from the readiness with which iodine is given up, poisonous symptoms may follow the use of even small quantities.

10DO-SALICYLIC ACID .- A compound of iodine and salicylic acid in which one atom of hydrogen is replaced by one of iodine. It contains fifty per cent. of iodine. A di-iodo-salicylic acid is also prepared, in which two atoms of hydrogen are replaced by iodine. It contains two parts of iodine in three of the compound. They are white, fine, crystalline powders, slightly soluble in water, soluble in alcohol, ether, fixed oils, and collodion.

They possess the combined action of iodine and salicylic

acid, and are said to be very serviceable antiseptics. ternally, in doses of from twenty to sixty grains daily, they have proved serviceable in rheumatism and have succeeded in relieving the fever and pain when the other

salicylates have failed. Sodium di-iodo-salicylate.—This salt occurs in white needles, and is recommended as an antithermic and antirheumatic. It is also said to be of great value as a local application in parasitic affections of the skin. The dose for internal administration has not been determined. Beaumont Small.

IODOSULPHATE OF CINCHONINE. - (Synonym Antiseptol.) This compound contains fifty per cent. of iodine. It is a very light, brownish powder, odorless, insoluble in water, alcohol, and chloroform.

It is an antiseptic and is said to prove serviceable in all conditions in which iodoform and similar compounds are employed. It may be combined with powdered talcum, one part to two; or mixed with vaselin or lanolin, Reaumont Small one part to ten.

10D0ZEN (C.H.2I.COOCH.3ONa) is an iodine derivative of methyl salicylate. It is used as an antiseptic externally and as an alterative internally.

IPECAC.—IPECACUANHA.—The dried root of Cephaëlis Ipecacuanha (Brot.), A. Richard. [Uragoga Ipecacuanha (Brotero) Baillon (fam. Rubiaceæ).] U. S. P. It is doubtful if this definition, for reasons given below, should not be made to include the lower or prostrate portions of the be made to include the lower or prostrate portions of the stem also. The name of this drug, which is adopted into most European languages, is borrowed from the South American Indians, by whom it is used to designate, not only this, but several other emetic roots. *Poaya* is another Bazilian name, also rather loosely applied to other roots besides the one under consideration. "Ipecac" is a roots besides the one under consideration. natural and convenient abbreviation.

The plant from which this drug is obtained is a low, semi-gregarious shrub, growing in the deep tropical woods of Brazil, with partly creeping stems and thickened

annulated roots. The roots, several in number, are long, tortuous, simple or slightly branching, white and filiform when young, but at maturity thickened to three or four times the diameter of their woody columns by the accumulation of starch-bearing tisue in the bark. This occurs in crowded, narrow, irregular, and generally incomplete, transverse rings, separated by deep, also incomplete, circular fissures, and is greatest in the middle portion of the root, which tapers toward each end, especially the lower. The woody column does not take part in either the rings or furrows of the bark. The stems of Cephaelis are of soft woody, sometimes almost herbaceous, texture; rounded, smooth, creeping, and rooting below; ascending, square, pubescent, and green above, with well-marked nodes and pubescent, and green above, with wen-marked nodes and leaf scars. It is this lower, rounded portion, lying shaded and for the most part covered by forest débris, which has practically the same composition and properties as the root, and which might be, and commonly is, used

with it. The remaining portions of the plant are well illustrated in the accompanying cut, which, however, does not show the prostrate habit of the basal portion of

HABITAT.—The district of Matto Grosso, in western Brazil, is the principal source of ipecac; but the plant grows also in the adjoining parts of that country as well as of Bolivia. The ipecac plant has been long cultivated as an object of interest in botanical gardens, especially in that at Edinburgh. Mr. McNab made the important discovery that it could be propagated by minute fragments of its roots, or even of its leaf stalks. By means of this plan a large number of plants has been obtained and sent to India and elsewhere for experiments in regard to its practical cultivation; so far, however, because of the slowness of its growth and the smallness and consequent expensiveness of the yield, its culture has not been commercially successful, and we are still obliged to rely upon its native country for our supply. It is collected by the Its native country for our supply. It is conected by the Indians in Brazil throughout the year, but mostly during the wet season, when the ground is soft, by simply grasping the stems in one hand and prying out the roots with a pointed stick held in the other. The gravel is then shaken out and the roots are dried in the air. When dry, they are sifted and sorted and packed in serons (bales made of hide) for transportation. It is mostly bought up by travelling traders, and suffers much exposure during their journeys, so that much of it reaches us in a mouldy and damaged condition. Ten or twelve pounds per day is said to be a good average collection. pecac collection is exceedingly irritating to the hands, especially the finger ends, as well as to other parts of the body, and is hence very objectionable to the laborers.



Fig. 2952.—Ipecac Plant. (Reduced about one-third.) (Baillon.)

The modern high price for rubber having afforded a profitable opening, its collection is preferred, and the price of ipecac has on this account very greatly adHistory.—The following paragraph is condensed from Flückiger and Hanbury. A doubtful reference to ipecac is made in an old treatise upon Brazil, published by Purchas in 1625. Piso and Marcgraf (1648) described it, and

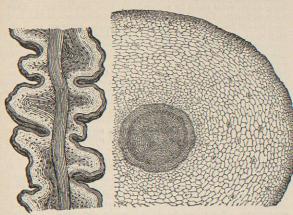


Fig. 2953.—Longitudinal and Transverse Sections of Inecac Root.

stated that it was in common use in Brazil. It was first carried to Europe in 1672, and its usefulness established by Helvetius about 1686, who kept its identity a profound secret until he received from Louis XIV. a handsome price for publishing it to the world in 1688. This carly use of ipecac was not as an emetic, but in the treatment of dysentery, which is still its principal employ ment in tropical countries.

OFFICIAL DESCRIPTION. -In pieces of indefinite length rarely exceeding 15 cm. (6 in.), and 3 to 6 mm. (1 to 1 in.) thick, curved and sharply tortuous, almost free from rootlets; surface red-brown or brown, occasionally blackish-brown, rarely gray-brown, closely annulated and usually exhibiting transverse fissures through the bark, their sides vertical; fracture short, the very thick easily separable bark grayish, usually resinous, the thin wood vellowish-white, without vessels; odor very slight, peculiar; taste bitter and nauseous, somewhat acrid.

When very thick, of a dull-gray color, with thin, merging annulate and with many starch grains exceeding 12 or 14 μ it is from Cephaëlis acuminata Karst., and should be rejected.

When ipecac is sound and free from mouldiness, its when specae is sould and free from mountless, its quality is proportionate to the thickness of the bark and the thinness of the ligneous portion.

The bark of ipecac consists entirely of thin-walled, polyhedral cells scarcely longer than broad, and pretty well filled with clustered and faceted starch grains, solitary grains rarely reaching a diameter of 12 or 14 μ . Liber wanting. All the medicinal activity of the drug resides in the bark, the wood being worthless and nearly

ADULTERANTS AND SUBSTITUTES.—The adulterants of and substitutes for ipecac have been so numerous and important that works have been written upon the sub-All have now practically disappeared, so far as the American market is concerned, with the exception of Carthagena Ipecac, the root of Cephaelis acuminata Karsten, of Colombia. This root is collected and sold, under the name of ipecac, upon a scale almost as ex-tensive as that of the genuine drug. Although sup-posed to be excluded by the United States customs laws, it does enter to a very considerable extent. In its ordinary form, it is readily distinguished, being a half or more larger of a dull brownish-gray color, less strongly annulated, and especially less deeply constricted between the annulations. The writer has seen the process in operation, in London, of selecting the pieces in which these

distinctions are the least marked, and staining them for the American market. The fractured surface is less distinctly white, being rather of a horn-grayish white, and the powder shows a similar difference. In the latter, the starch grains reach a much greater size and are more inclined to be solitary. It is very questionable if this root is inferior to the genuine, or if it should not be admitted to the Pharmacopæia. Its percentage of total alkaloid is commonly a little greater than in the genuine; but the composition of this alkaloid, or rather its physiological and therapeutical action, is so uncertain that it has been refused admission to the recent edition of the British

Composition.—The medicinally unimportant constituents of ipecac are a large amount of starch and calcium oxalate, and small amounts of pectin, sugar, and resin. The important constituents are ipecacuanhic acid and the alkaloids, namely, caphaëline, emetine, and a third not yet studied, the three alkaloids together existing to the extent of about two per cent. Of this total, the emetine constitutes about three-fourths, the cephaëline about onefourth, the third being in very small amount. In Carthagena ipecac, the cephaëline is about three-fifths, the emetine about two-fifths. The physiological and thera-peutical importance of the ipecacuanhic acid and of the third alkaloid is not known, but there are special reasons why it is in great need of investigation, especially that of the former substance. There is nothing in the action of either emetine or cephaëline to explain the repute of ipecac in the treatment of dysentery, a repute strong and general as to demand recognition. This effect appears to be secured, moreover, after the removal of the alkaloids, and it would appear that it must be due to the bitter acid, which is in reality a glucoside.

Cephaëline ($C_{14}H_{19}NO_2$) is separated from Emetine ($C_{14}H_{18}(CH_3)NO_2$) by the use of an aqueous solution of caustic alkali, the emetine being taken up

from it by ether.

ACTION.-Ipecac (and still more the alkaloid) is a modeaction.—Ipecae (and still more the alkalold) is a moderate local irritant, producing smarting, redness, and, if a long-continued application is made to the skin, finally, troublesome pustulation. The powder of either, inhaled, produces sneezing, stinging, and increased secretion from the nostrils and deeper air passages; in susceptible persons a severe coryza may be simulated. In experiments upon animals, diarrhea and even dysentery, with bloody discharges and inflamed intestinal mucous membranes have followed large doses. It is thus evident that local stimulation, or irritation at least, forms a very characteris tic part of the action of ipecac. This is also seen in the pain and inflammation, frequently abscess, at the point of hypodermic injection, on account of which this mode of use is not available. As to the systemic effects when thus introduced into the circulation, it is to be noted that n fatal cases severe inflammation of the lining of the stomach and intestine has frequently been observed all the ndications being that it has resulted from excretion of the alkaloids into these organs. Irritation of the pulmonary tissue, which is often severe, is apparently due to a similar excretion there. The emetic action of the drug, as well as the salivation and nasal discharge, could thus be readily explained on the ground of local irritation. When the alkaloid is taken, it is distinctly noted that there are two periods of gastric disturbance, one following the other at an interval of about thirty minutes. It has been thought that this second attack was due to central action, after the alkaloid had become absorbed; but it is at least possible that it follows its re-entrance into the stomach upon excretion from the circulation. Whether the emesis of ipecac is purely a local effect or partly of central origin, is the most important question concerning It is notable that the disturbance of emetine is les than that of cephaëline, of which latter emetine is a methyl compound; and we know that methyl compounds are often less energetic irritants, or are even sedatives, to the centres. This would seem to indicate central activity.
This question is not of practical importance, as the general effects of the drug are clear and evident. When taken