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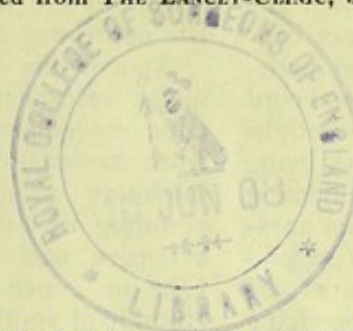
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CATHARTICS HYPODERMATICALLY.*

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Podophyllin may be taken as an example of a group of vegetable cathartics, solutions of which, either introduced under the skin or intravenously, occasion increased peristalsis. Podwissotsky has found two active principles in podophyllin—a neutral crystalline substance known as podophyllotoxin ($C_{23}H_{21}O_9$) and picropodophyllin. The official resin of podophyllin consists of two resins, one soluble in both ether and alcohol, the other in alcohol alone. Squibb describes podophyllotoxin as a yellowish-white, very bitter powder, soluble in alcohol, partially in ether and chloroform, drastic cathartic. Dose by the mouth, one-twelfth to one-eighth grain (0.005 to 0.008 gm.) in alcoholic solution. Podophyllotoxin injected under the skin of an animal or man causes a purgation in from twenty minutes to an hour. The injection of one-fifth grain under the skin of a terrier produced seven liquid stools within three hours. Podophyllotoxin injected under the skin of a cat and the cat killed a few hours later, the gut from near the stomach to the large intestine shows marked congestion. If the mucous membrane and contents of this portion be extracted with alcohol a solution is obtained which possesses the properties of podophyllotoxin. The local irritation of this drug, when used subcutaneously, is such that it cannot be used indiscriminately. This objection holds with solutions of the other vegetable cathartics which act when used hypodermatically, such as aloes, senna and colocynth.

Salicylate of eserine has been studied by Craig, of Boston, and Vineberg, of Mt. Sinai Hospital, New York. They used it in milligramme doses hypodermically every three hours, producing catharsis in 50 to 75 per cent. of cases. It acts on the muscular coat of the intestine like ergot on the muscles of the uterus. It does not pour out fluids

into the intestine. It will not act if the muscles of the intestines are so distended with gas that they are paralyzed,

Mackenzie and Dixon (*Edinburgh Medical Journal*, November, 1898), report numbers of experiments with podophyllotoxin hypodermically in cats, dogs and men, resulting in copious evacuations in about one-half hour.

Atropine has been known to produce peristalsis in some cases when used hypodermically. It is not likely to come into favor because of its other action on the secretory glands.

THE MORPHINE GROUP.

Morphine injected in large doses induces purgation and vomiting in some cases. Apomorphine is a powerful emetic, but has little effect on the intestine. Codeine produces purging in animals more readily than morphine, whilst apocodeine brings on purging without any vomiting.

APOCODEINE HYDROCHLORIDE.

Guinard showed first that vomiting did not follow its use, as in the case of apomorphine. Murrell experimented with it and discovered that it was of value as an expectorant. Roviart used it subcutaneously in patients suffering from constipation, and reported in its favor. Two c.c. of a 1 per cent. solution of apocodeine (about $\frac{3}{8}$ grain), injected under the skin of a man produced one or two soft motions in an hour. There is no feeling of nausea, and a slight irritation at the seat of the injection passes off in a short time. Experiments on animals go to show that apocodeine acts diametrically opposite to nicotine—that is, it causes vaso-motor dilatation, fall of blood-pressure, increased peristaltic movements. The absence of effect on the stomach by apocodeine may be explained by

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the fact that the sympathetic gives few if any fibres to the stomach. It cannot act centrally on the brain because increased peristalsis can still be seen when the vagi and cord are cut; nor can it act on the extreme periphery, for when applied directly to the living intestine all movements cease. On injecting moderate quantities of this remedy into anesthetized cats and dogs or rabbits it is easy to show that certain ganglionic cells are paralyzed. After the injection of apocodeine stimulation of the chorda gives no increased submaxillary secretion, although the secretory neurons are active, because the exhibition of pilocarpine still gives rise to a greatly augmented secretion. We infer from this that the ganglionic cells are paralyzed on the chorda tympani.

Magnesium sulphate injected subcutaneously into an adult person will cause purgation. It is needless to say that this effect is produced in an entirely different way from that by the mouth. Magnesium sulphate administered by the mouth causes no increase in peristalsis, but acts by the increased amount of fluid which it attracts into the intestines. The hypodermic injection causes increased peristalsis. The injections are generally made in the arm and in doses of one and a half grains of a 2 or 3 per cent. solution. This result occurred only in a majority of the cases, and a further objection is its supposed toxicity if directly injected into the blood.

Digitalis, pilocarpine, physostigmine and muscarine produce this effect when administered hypodermically in sufficient doses, but the ill-effects which accompany them prevent their use in this way for this purpose. Colchicine has been suggested and tried, but has been cast aside on account of its simultaneous

action on the stomach and its insidious and late depressing effect on the medulla.

Apocodeine lowers blood pressure, produces vaso-dilatation, and increases peristaltic movement. This all occurs probably from its sedatory action on the sympathetic inhibitory ganglia. It does not produce vomiting or other ill-effects and merits an extensive trial as a hypodermic purgative. One or 2 per cent. solution of the hydrochloride of apocodeine should be used, which solution should be filtered and neutral. Two or three cubic centimetres should be injected for a dose.

Experiments with apocodeine hypodermically have been made on an extensive scale by Prof. Combemale, of the Lille University. In his hands the injection of thirty minims of a 1 per cent. solution of apocodeine hydrochloride was followed in almost every instance within half an hour by one or two loose stools. The only bad effect he found was some irritation of the skin at the site of the injection, which was avoided by injecting the drug deeply into the muscular tissue.

A satisfactory subcutaneous purgative is a want seriously felt in medicine—for example, in such conditions as inflammation of the stomach when that organ is so sensitive that it will not retain a purgative. In apoplexy, coma and unconsciousness, obstruction to the esophagus or refusal of the patient to take medicine, and after certain operations, a drug which could be administered subcutaneously satisfactorily would be of the greatest advantage. Many pharmacologists and manufacturing chemists have been and are studying this subject and experimenting with it, but so far with varied success.