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ABSORPTION AND ELIMINATION OF THESOME COMMONLY USED DRUGS,

Dr. Charles G. Kerley, New York City, took issue with Professor Lane in regard to the supply of milk to poor people. They do not know what good milk is. They have the

WITH PRACTICAL DEDUCTIONS FROM A KNOWLEDGE OF THE SAME.

least money and the most babies, and the state is in duty bound to protect the offspring of the poor. This work is for the protection of these poor children who have no means of protection from their own people, because of the unfortunate situation in which they are born, and which is no fault whatever of theirs.

E. R. ZEMP, M.D.

Dr. A. C. MERCER, Syracuse, N. Y., made a suggestion, and that is that physicians insist that pasteurized milk is simply renovated milk. This pasteurized or renovated milk business he said, may be likened unto a lady going to a bonnet shop and buying a bit of ribbon and trailing it through the mud on the way home, then trying to wash and iron it and put it on a hat, instead of keeping it clean from the beginning.

Professor of Materia Medica and Therapeutics, Pediatrics and Clinical Medicine, Tennessee Medical College. KNOXVILLE, TENN.

DR. ALEXANDER MCALISTER, Camden, N. J., referring to the sale of skim milk, said that there is a law in Pennsylvania and New Jersey requiring that all skim milk be labeled, and any milkman found selling skim milk without being labeled as such is fined.

It is a regrettable fact that many physicians prescribe drugs either from habit or from hearsay. Even with the drugs prescribed many times daily some of their important actions are unknown or forgotten.

DR. HENRY E. TULEY, Louisville, Ky., thought that Washington is many years behind the times. With the many departments of the government at its command, it should have begun this work long ago and been an example to other cities of what good could be accomplished. As to pasteurization, New York City, he said, has disposed of the question of wholesale pasteurization most satisfactorily. The health department of that city, after conference with members of the medical profession and the milk commissions, has asked for a large appropriation, something like \$1,000.000, which is to be expended in the inspection of dairies. This is a wise decision and it is believed that the result will justify this large expenditure. At a conference of medical milk commissions the Cincinnati members reported the results of a very interesting investigation of milk delivered to several hospitals and its condition when it reached the various floors for distribution to the patients. The increase in the number of bacteria between the time of its delivery to the hospital and when delivered to the patients was enormous. Dr. Tuley is convinced that public opinion is a difficult thing to arouse, in spite of what has been said. It is especially difficult to educate the poor in regard to milk. An important item to them is the cost of the milk. It is absolutely impossible to produce a clean, cold, wholesome milk cheaply. The question of the price of certified milk has agitated the Louisville Milk Commission not a little. The price has been placed at 10 cents a quart to consumers. The producer gets 25 cents a gallon, the distributor 15 cents a gallon. Both the producer and the distributor are under control of the milk commission. A clean, cold milk can not be produced for less than 8 cents and possibly 10 cents a quart. Milk fit for consumption can only be had at prices cheaper than this when philanthropic people and societies aid the poor. The question of tuberculosis in dairy cattle is most important, and Dr. Tuley urged that the public

Certainly it is not necessary for me to state that a knowledge of the absorption and elimination of drugs is required before they can be administered intelligently. The fact that a physician is prevented from overdrawing his mortality account by an indulgent Providence should not make us any the less eager to bring about an improvement in a condition so easily improved. The trouble is we do not study our materia medica enough. Many of us get our ideas of therapeutics from works on practice. This is sufficient to a degree only. The knowledge obtained from such a source can not replace the knowledge of the physiologic actions of drugs that should be the basis of our therapeutic efforts.

Special Diets in Hospitals.-A committee was appointed by the French authorities, in 1903, to suggest modifications in hospital diets. The recommendations of the committee were adopted and attempts have been made to introduce them gradually in the Cochin Hospital. Eight different diets were proposed by the committee, the diet for healthy persons, for convalescents, for dyspeptics, for the tuberculous and for diabetics, the milk-vegetable diet, the exclusive milk diet and the salt-free diet. The results have been eminently satisfactory. The salt-free diet is a recent suggestion on the part of the committee, as also the addition of bouillon to the diet for the tuberculous. The committee urges that roast meat should be ground fine for dyspeptics, and that the articles of food in the salt-free diet should be varied to render it as appetizing as possible. The latest report of the committee was published in the Bull. Soc. Méd. des Hop. for June 28 and July 5, 1907.

be educated to the dangers which lie in a milk supply coming

from a non-tuberculin tested herd.

That the systemic action of a drug is due to its absorption can not be disputed, and that the duration of its action is dependent on its elimination or oxidation is equally true. Drugs in the stomach produce no effect outside of local and reflex actions. It is only when they gain access to the system at large that their influence is felt. The knowledge of the rapidity with which a drug is absorbed and eliminated carries with it the knowledge of how often to repeat the dose of that drug. To prescribe a drug that is exceedingly fleeting in its action at long intervals is as absurd as it is dangerous to prescribe at short intervals a drug that is slowly eliminated. Knowing the relation of the drug to both of these processes gives us a happy control over its action.

The rapidity with which a drug is absorbed depends on a number of conditions. As a rule, the more soluble the drug the quicker is it absorbed. Alcoholic solutions are more rapidly absorbed than others. Drugs in solution when served hot are introduced into the system more rapidly than when served cold. Some drugs are so irritating to the stomach that the local disturbance produced entirely prevents absorption. Some drugs, but poorly absorbed themselves, form in the intestinal tract compounds that are rapidly and easily absorbed. much for the drug.

As to the patient, the chief factor influencing absorption is the circulation. If the circulation is active absorption will be active. If the circulation is sluggish absorption will be slow. It may be entirely suspended. Absorption is peculiarly slow in dropsical conditions so that hypodermic medication is at times not only uncertain, but absolutely dangerous, for the various doses remain in the tissues for days only to be absorbed with the exudation after severe purgation, active diuresis or tapping. In this way the patient gets at one time all that has been given for several days. This could easily prove fatal, especially when the generally weak condition of this class of patients is considered.

The condition of the stomach and intestines markedly affect the absorption of drugs. It is apparent that a chronic inflammation of the stomach, with its accompanying coat of viscid mucus, will retard absorption. The same is true of acute inflammatory conditions. Some drugs are not absorbed from the stomach at all, but owe their effect to the fact that they are passed into the intestines where absorption is active. Thus it is that the motor function of the stomach affects absorption, while an active peristalsis may carry the drug so rapidly through the intestinal tract that but little of it is absorbed. An empty stomach absorbs rapidly; a stomach filled with food absorbs more slowly.

The skin can not be penetrated by many drugs, while others pass through readily and easily. We take advantage of this fact in the treatment of certain diseases, especially where we wish to spare the stomach. So prompt is the absorption of some drugs through the skin that toxic effects are easily produced; therefore, this means of administering drugs should not be used carelessly. It is hard to reconcile the possession of intelligence with the fact that physicians try to get effects, by local application, from drugs that have no power of penetrating the skin. Yet this is sometimes the case.

The fate of drugs after they gain entrance to the general system is an interesting study. Some of them are eliminated unchanged; some reappear in the excretions as compounds formed from the original drug, while others are oxidized. From a practical standpoint, in regard to systemic effect, it makes little difference how the effect of a drug is lost, just so we know that it ceases to act in a certain time. This knowledge permits us to regulate the doses that they will not overlap, thus avoiding the so-called accumulative action. On the other hand, we avoid the withholding of a drug much needed by the system by administering at short intervals one whose action is fugacious.

OPIUM.

Absorption.—Opium and all of its preparations are rapidly absorbed when given by the mouth. The effect of an ordinary dose can be felt in ten to fifteen minutes after it has been given. Given hypodermically its effect is much more rapid. Morphin given in this way can be detected in the saliva three minutes afterward. sudden is its effect when given hypodermically that one should be careful not to give too large a dose when administering it for the relief of pain, as the pain may suddenly stop and the full force of the drug be spent on the vital functions, causing death. One-sixth of a grain of morphin has caused death, so it is better to give small doses and repeat every half hour until relief is obtained, then stop, or give less often. Opium is not only readily absorbed from mucous membranes and subcutaneous tissue, but it is absorbed in a slight degree when applied locally to the skin; at least clinical proof leans a little in this direction. A case seemingly corroborative of this assertion is on record in which four grains of crude opium placed in the ear caused death.

Elimination.—The elimination of this drug is comparatively slow, a single dose taking about forty-eight hours to be completely eliminated. It appears in all the secretions, no matter how administered. After a hypodermic injection it is found in the urine, feces, sweat, tears, milk, saliva and gastric juice. It is these last two that are especially contaminated with it. Very little escapes by way of the urine. One-half the dose can be recovered from the stomach even when it has been administered under the skin, or by the rectum. In chronic opium eaters it can be obtained from the urine one week after they have been taken off the drug, and in one case it was found in the brain, liver and kidneys two

weeks after the last dose was taken before death ensued from other causes. Opium thus seems to have a cumulative action. The child in utero can acquire the habit from its mother constantly taking the drug.

Practical Deductions.—Large doses of opium should never be given; small doses frequently repeated are preferable. Opium applied locally has but little effect, and such as it has is probably of central origin. Given repeatedly or in large doses to nursing mothers it may cause alarming symptoms in the infant. When a mother who is a habitual opium eater gives birth to a child, the child may develop alarming symptoms about the second or third day. The child may go into collapse from the sudden discontinuance of its accustomed dose of opium. In opium poisoning one of the most important things to do is to keep the stomach free from the drug, as it is largely eliminated into this viscus to be reabsorbed. To accomplish this end the stomach should be washed out regardless of the way in which the drug has been taken. Or emetics with copious draughts of water may be given and the patient made to drink at short intervals a weak solution of potassium permanganate, which may be given freely without fear of doing harm. On the other hand, the hypodermic use of this solution is useless. urine, but more especially the saliva, can be used in making a diagnosis, as they both will respond to tests for morphin. This is important from a medicolegal standpoint, and in differentiating between opium poisoning, cerebral hemorrhage and acute alcoholism.

COCAIN.

Absorption.—This drug is used extensively and is a powerful agent for good and harm. It is absorbed with remarkable rapidity from all mucous membranes, but it can not penetrate the unbroken skin. As the ear from an external point of view is not lined with mucous membrane, it would seem that cocain must be absorbed with difficulty, if at all, when placed in the auditory canal. Clinical experience strengthens this opinion, as ordinary solutions are almost useless for anesthetizing the drum. Cocain itself (the alkaloid) is soluble in fatty bases, but its salts are not. While this fact is of some practical import, it is not as important as some writers would have us believe, for, whether it is soluble or not, when placed in contact with a mucous membrane its effect will be felt. This can be demonstrated easily by making an ointment of cocain hydrochlorid and then placing a little of it in the rectum. The pain from a fissure or ulcer is promptly relieved temporarily. Solutions of cocain are more readily absorbed from the nasal cavities than from any other part of the body; the eye comes next, while the mouth and male uretha are not far behind these. The rectum and vagina offer much more resistance to the passage of this drug into the system. The effect of the drug when applied to these susceptible areas is felt in half a minute. Hypodermically its effect is almost instantaneous. A girl of 12 met death in forty seconds from a hypodermic injection of twelve drops of a 4 per cent. solution. Death has occurred from rubbing a little of a 5 per cent. solution on the gums, and a 4 per cent. solution applied for toothache has caused death. One fact stands out prominently in connection with the use of cocain in the eyes and nasal cavities, and that is that very often the systematic effect obtained is out of all proportion to the amount of drug used. This is explained by Corning in the following manner: Remedies applied to the nasal mucous membrane reach the brain, and especially the cerebral cortex, in a more concentrated state than when administered in other ways. Even though the amount of medicinal substance may not be great, its increased concentration at the seat of its action must of necessity result in physiologic effects out of proportion to the amount used. It is supposed that the drug reaches the brain in this concentrated state by being taken up by the vessels that penetrate the lamina cribrosa.

Elimination.—Cocain is eliminated rather rapidly, chiefly by oxidation. A small amount escapes by way of the kidneys.

Practical Deductions.—In case of a patient on whom corain has never been used, the physician should exercise caution and should have close at hand alcohol and ammonia to use in case symptoms of collapse arise. He may not need these stimulants often, but sometimes he will, and need them quickly. When the drug is injected into the tissues to produce anesthesia, if the part of the body permits, a ligature should be thrown around it in order to keep as much of the drug as possible from entering the general system. After the operation is completed the ligature should be removed gradually. It is advisable to let the wound bleed freely before coapting it, in order to wash out as much of the cocain as possible. Cocain is of but little value, if any, in earache. To cocainize the ear drum equal parts of cocain, menthol and phenol should be used. A few drops of this mixture may be dropped into the ear shortly before operating. Strong solutions should not be used ordinarily in the eye, nose or mouth, but they can be used with impunity in the rectum and vagina, as solutions of less strength than 10 per cent. have but little influence in these localities. In dropping solutions of cocain in the eye care should be taken that they do not run down into the nose through the lachrymal duct. This can be prevented by pressing on the duct with the finger, or holding the patient's head so that the solution runs out of the external canthus. Excessive dosage should not be used in applying the drug locally.

DIGITALIS.

Absorption.—The absorption of digitalis is exceedingly slow, no matter how it is given. When given by the mouth hours and sometimes days may elapse before its full effect is obtained. It is absorbed by all mucous membranes, although it is more or less irritating to them; it is also rapidly absorbed by the skin.

Elimination.—While its absorption is slow, its elimination is more so; consequently, the drug accumulates in the system and may manifest itself suddenly by the onset of toxic symptoms. As it is used in conditions in which the circulation is disturbed, this, no doubt, contributes to the slowness of its action. How it is eliminated is not positively known. It probably escapes by way of the kidneys, but the larger part of it is supposed to be oxidized in the system.

Practical Deductions.—We can not rely on digitalis in cases of emergency, where it is necessary to stimulate the heart quickly. In these cases we should resort to the simultaneous use of alcohol, or ammonia and digitalis, for about the time the diffusible stimulant is waning the digitalis will begin to take up the work and carry it along for some time. Care should be exercised in draining off dropsical effusions in patients who have been taking large doses of digitalis for some time. The sudden withdrawal of the fluid may cause the absorption of enough of the drug to poison the patient. As digitalis is irritating to mucous membranes, it should not

be given by the mouth to patients suffering from acute gastric troubles. In these cases a hot poultice made from the leaves can be applied to the loins, and in this way the physiologic action of the drug can readily be obtained. Most preparations of digitalis are precipitated into the tissues when given hypodermically. This accounts to a certain degree for the slowness of its action when given this way.

NITROGLYCERIN.

Absorption.—This drug is mentioned here to contrast it with digitalis. These two drugs occupy the extreme ends of the scale in regard to the time of action. Digitalis is slow; nitroglycerin is quick. Nitroglycerin is absorbed almost instantly after coming in contact with a mucous membrane. So rapid is its action and so powerful its effect, it should never be "tasted," as death may result. One drop of the official solution has proved fatal. The full effect of this drug is ordinarily felt in from two to five minutes after it is administered and is maintained for about forty-five minutes.

Elimination.—It is eliminated by way of the kidneys and breath.

Practical Deductions.—This drug may be used when a quick effect is desired to relieve severe pain due to muscular spasm, as in angina pectoris. In all cases where it is given for its relaxing effect on the circulation, as in cases of high arterial tension, it should be administered at short intervals. It is useless to give such a drug as this three times a day. Neither should it be combined with digitalis with the idea of overcoming the contraction of the arterioles caused by the latter, for the effect of the one is brief, while the other is greatly prolonged. This counteraction, however, may be obtained by giving the nitroglycerin separately and at the proper intervals.

BELLADONNA.

Absorption.—This drug is rapidly absorbed from mucous membranes and skin. After a dose of atropin has been given its effect is manifested in a few minutes.

Elimination.—Its elimination is rapid by way of the kidneys and intestines; therefore, we need have no fear of a cumulative action. It can be found in the milk of nursing mothers, especially when they are in poor health, for the milk in these cases assumes the character of an exudation rather than a secretion. The effect of a single dose lasts for two or three hours.

Practical Deductions.—In using atropin in the eye the solution should be kept from running down into the nose through the lachrymal duct, as a number of cases of poisoning are on record from this cause. In giving belladonna to nursing mothers the baby should be watched; especially is this true if we are giving large doses and the mother's health is poor. Remembering this will enable one to account for certain symptoms in the infant that otherwise might prove perplexing. In making local applications of belladonna ointment the patient should be instructed to wash the ointment off if marked dryness of the mouth and dilatation of the pupils occur, as enough of the drug can be absorbed through the skin to poison the patient. If we suspect that a patient has been poisoned by belladonna a positive test can be made by dropping some of the urine into the eye of a cat, when dilatation of the pupil will occur if our suspicion is correct. This is important from a medicolegal standpoint. In poisoning from belladonna the urine is retained, so the patient should be catheterized for it is possible that reabsorption may take place from this viscus. However, we catheterize more particularly to prevent overdistension of the bladder.

CHLORAL.

Absorption.—The effects of this drug are manifested quickly (within five minutes) after its ingestion, and last several hours. It is readily absorbed from all mucous membranes if not given in too concentrated form. It is irritating to both skin and mucous membrane, although later it is anesthetic in its effect.

Elimination.—It is eliminated by way of the kidneys, partly as chloral and partly as urochloralic acid. Such urine is capable of reducing copper solutions. Chloral has no cumulative action; it circulates in the blood as chloral. It was once thought that the alkalinity of the blood caused a breaking up of this drug in the system into chloroform and formic acid, but while this change does take place in the test tube when chloral is treated with an alkali in solution, the probabilities are that no such change takes place within the body. Chloral is also eliminated by way of the skin, producing at times a variety of skin lesions.

Practical Deductions.—Chloral should always be given well diluted, and as a rule infants should receive it by rectum. As it is eliminated as chloral, and as chloral is irritating, it should not be given in acute inflammatory conditions of the kidneys. Being rapidly absorbed, it is better to give small doses at short intervals, say every hour, than to give one large dose, especially as patients vary considerably in their susceptibility to its effects. In examining the urine of patients who have been taking chloral for a long time, or in large doses, bear in mind that a reaction with Fehling's solution does not necessarily mean sugar in the urine, for certain compounds of chloral found in the urine are capable of reducing copper solutions.

IODOFORM.

Absorption.—In itself iodoform is a non-irritating substance, but by decomposition and the formation of new compounds it becomes active. It is absorbed slowly from the alimentary tract, but from wounds it is taken up with comparative freedom.

Absorption is much more rapid when applied to wounds, so that poisoning readily takes place after its free use if the denuded area is large. There are several varieties of symptoms that arise from its absorption. There may be simply high fever, or high fever with rapid pulse; rapid pulse without fever, collapse and death, or the symptoms may closely resemble those of meningitis. Especially may any of these symptoms arise if iodoform is used within the peritoneal cavity, for here its absorption is certain and rapid.

Elimination.—The iodin escapes from the body by all the secretions and even by the breath, not as iodin, but as iodids, iodates and organic compounds. The elimination begins soon after ingestion, but is carried on slowly, so that it can be found in the urine three days afterward.

Practical Deductions.—Iodoform should not be dusted freely over large areas of denuded skin. It should be dusted with care within the abdominal cavity. As it is eliminated through all the secretions, babies may get it through the milk of their mothers when they are using the drug freely. In surgical cases the attendant should be on his guard when iodoform has been used and any alarming symptoms should not be credited to shock, hemorrhage or infection until the possibility of iodoform

poisoning has been eliminated. It is possible that patients have died from poisoning by this drug and the case diagnosed as one of the above-mentioned conditions. It is said that a quick diagnosis can be made by placing a silver quarter of a dollar in the patient's mouth. If iodin is present a taste of garlic is experienced; or a little saliva can be mixed with calomel, when a canary yellow precipitate is formed, due to the formation of iodid of mercury. When the pulse quickens, or the temperature rises, or the patient shows signs of distress after iodoform has been freely used, it is best to remove the drug and give the patient copious drafts of water. In the severe cases the prognosis is very bad, no matter what line of treatment is carried out. Iodoform by the mouth in ordinary doses very rarely causes alarming symptoms.

THE PARAFFIN INJECTION TREATMENT OF INGUINAL HERNIA.*

M. L. HARRIS, M.D. CHICAGO.

It is more than fifty years since attempts were first made to cure ordinary rupture or inguinal hernia by injecting some irritating fluid into the sac or into the tissues surrounding the neck of the sac.

The method was originally introduced by the regular profession, but it did not take long to demonstrate not only that it was unsuccessful in the majority of cases in so far as effecting a cure was concerned, but also that it was not so free from risk as was at first supposed. While the materials composing the injecting fluids have varied somewhat, according to the fancy of the particular operator, the effect of them all is practically the same, namely, to excite an inflammatory exudate which is expected to block the hernial opening and thus to prevent the descent of the hernia.

As new-formed connective tissue thus excited by means of local irritants is not entirely permanent but usually readily yields to pressure, the results following this treatment are so transitory and so unsatisfactory as not to warrant a continuance of the method by the regular profession. However, the simplicity of the method and the fact that it can be performed without the use of a knife and without laying the patient up, made it popular with the advertising and itinerant charlatan, whose thoughts are more centered on the fleecing of his victim than on the cure of the hernia.

As a result surgeons are almost continually called on to operate on patients with hernias who but a short time before were unsuccessfully treated by the injection

About seven years ago Gersuny introduced the injection of paraffin into the tissues for a variety of purposes, one of which was the cure of hernia. advantage claimed for the paraffin as an injection material was that, as it is insoluble in the tissues, it remains where placed practically indefinitely and, therefore, the effect is more or less permanent. The method was readily adopted by the profession and its application extended so rapidly that in 1904 Krlin already had tabulated thirty-six distinct indications for its use.

It was not long before accidents following the injections began to be reported. These consisted principally

^{*} Read in the Section on Surgery and Anatomy of the American Medical Association, at the Fifty-eighth Annual Session, held at Atlantic City, June, 1907. 1. Arch. f. klin. Chir., lxxiv, 915.