DR. C. W. BURR, Philadelphia, said that he did not mean that in a man whose brain was occluded through the obstruction of an artery due to syphilitic disease iodid of potassium would dissolve that softening and create a new brain, and hence bring about restoration of function. He meant that in syphilis there may be syphilitic arthritis, not sufficient to produce softening of the brain, but quite sufficient to interfere with the function and to produce aphasia which, under the administration of mercury and iodid, certainly does clear up.

DR. W. J. HERDMAN, Ann Arbor, said that this whole matter can be summed up in the simple statement that while educational methods are the best to employ when there is any capacity left after injuries or organic disease of the different sorts, yet it is this capacity for recovery that is really the condition which determines how far the recovery will take place. There are some cases in which one would not by any process of education expect any degree of improvement. There are other cases which do possess such a capacity for improvement, and the individual will no doubt, without any very great help, show progress for the better, but it is the physician's business to employ therapeutic measures so far as they are helpful. Whether it is called a "grammatical process" or not, there is no question that the aphasic, if he retains any capacity in language, retains the vertebræ of that language, and in order to make it more ornate and intelligible he must, of course, place on the vertebræ the soft parts. Dr. Herdman does not agree with Dr. Langdon that the instruction of the aphasic must proceed along the same lines as the instruction of a child. The whole possibility of development in an aphasic depends on what remains of what actually did exist there, and in arousing this into action again. If the capacity never existed it could hardly be expected that the patient could be educated beyond the stage of his former acquirements; if the capacity does, or did exist, then the process of a systematic attempt at education is exceedingly helpful.

DR. CHRISTOPHER C. HERSMAN, Pittsburg, said that it is true that language is used in spite of grammar, and that after language has been learned it is perfected by grammar. If the patient is word blind and has to be taught words, he also needs synthetic teaching, or instruction in synthesis, building up, as well as teaching the individual words, and while teaching him the words, if the construction is also taught, more thorough advance is made than by simply teaching him the words.

DR. CHARLES K. MILLS said that the method of re-educating the aphasic is not exactly that which is applicable to children. The aphasic has both an advantage and a disadvantage as compared with the child. His advantage over the child is that his brain was thoroughly organized and in some cases thoroughly educated before the occurrence of the lesion; his disadvantage is that the child in its education started out with a potential mechanism of speech not affected by disease. Dr. Mills, of course, has taken the nature and extent of the lesion into consideration. He has seen cases of gummatous meningitis with aphasia and without other symptoms, the aphasia disappearing under the action of iodid. The first patient may have had a specific infection, but there was something more, a destructive lesion of the language center, and it is for this that he requires re-education. Dr. Mills has seen uremic aphasia and aphasia due to all sorts of affections which are remedied and do remedy themselves in time, but the remarks here apply to cases not to be restored to speech by time or medication. Dr. Mills stated that one inference drawn from part of the discussion is that these patients would get well anyhow by the progress of time in proportion to their natural, plus their acquired capacity, before the aphasia; but this is not quite true, as he knows from a long experience. He used the term grammar in a rather broad sense, in order easily to convey his idea. The patient must be restrained in the use of language as he formerly used it. There is a grammar of the slums. If a child who lives in the Bowery and uses the language of Jimmie Fadden becomes aphasic, he must regain this particular sort of language. The method

of training must not be simply a method of memory. The patient must learn again the use of prepositions, adjectives, conjunctions, and auxiliaries, of all the parts of speech that go to make up sentences, and the methods of arranging these in sentences for the expression of thought.

THE CONTROL OF INTERNAL HEMORRHAGE BY DRUGS.*

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By the term internal hemorrhage, as used in this paper, I include all forms of bleeding in which the bleeding point is not within reach of direct topical application.

It will be my purpose to set forth the general principles on which rational medical treatment is based, and not to discuss the relative merits of surgical and medical means.

In the first place, it may be stated that we have no specific remedy for the control of bleeding, and secondly that the employment of many of the drugs recommended is not based on rational grounds. As will be seen presently various agents are advised for a similar condition which act antagonistically, so that if one does good, the other must do harm.

The preference given to many remedies by clinicians is too often based on insufficient data. The action on a small series of cases of certain character may not apply to all hemorrhagic conditions, and the tendency of the bleeding to cease from nature's efforts is so important a factor that we are never sure our drugs have exercised any influence whatever.

In order to discuss intelligently the control of internal hemorrhage, I shall state the following general principles:

1. The mere onset of hemorrhage does not necessarily indicate medical treatment. The general tendency of bleeding is to cease from natural causes, and often more harm than good is done by overdrugging.

2. All patients, bleeding from whatever cause, must be kept in a state of absolute rest and quiet, bodily and mental, so far as this is possible.

3. All forms of hemorrhage may be more or less benefited by what may be termed collateral treatment. Change of bodily posture as indicated, drawing the flow away from the bleeding point as much as possible, the use of cold, heat, counter irritation, ligature of the limbs, etc.

4. The drug treatment of hemorrhage includes:

- A. First, the use of hemostatics, acting locally when this action may be secured, as in certain forms of bleeding in the gastro-intestinal tract. Second, the use of internal hemostatics.

- B. First, the use of drugs for the purpose of lowering the blood pressure, by depressing the heart or widening the blood paths. Second, the use of drugs to produce a local constriction of the vessels around the bleeding point.

In the consideration of the action of drugs on the vasomotor system we face one of the great difficulties of our problem. Vasoconstrictors to be of value must possess an affinity for the vessels around the bleeding

* Read at the Fifty-fifth Annual Session of the American Medical Association, in the Section on Pharmacology, and approved for publication by the Executive Committee: Drs. G. F. Butler, Solomon Solis-Cohen and O. T. Osborne.

point and there alone; otherwise a rise of general blood pressure will more than compensate the constricting action. The local constriction of the bleeding vessels may be brought about relatively by those vasodilators which act on the vessels of the general circulation, but do not dilate those of the bleeding area. The difficulties of the problem are obvious. Sollmann discusses briefly the selective action of dilators and constrictors, a knowledge of which is of paramount importance.

"The lungs are not much influenced by vasomotors. Hence dilatation would be indicated: Nitrites.

"The vessels leading to the brain are very subject to dilators, but not to constrictors. Neither measure would therefore be useful. If there is not naturally a showing, aconite would promise good results.

"The splanchnic area is the area most sensitive to vasomotor influence, and which reacts most promptly to either dilators or constrictors. The latter would be indicated: Strychnin or hydrastis.

"The skeletal muscles are not readily dilated nor constricted. Dilatation would be indicated: Nitrites.

"The uterus is strongly subject to constrictors. In postpartum hemorrhage, ergot; in menorrhoea, hydrastis and especially local treatment."

These general postulates urge me to controvert the internal use of all drugs producing a rise of general blood pressure, either directly as digitalis, or indirectly as the emetics, ipecac, etc., with the exceptions of ergot and hydrastis in bleeding from the uterus, and possibly in hemorrhages of the splanchnic area.

With these preliminary remarks I shall proceed to outline briefly the general action of some of the remedies advised as internal hemostatics. This will illustrate how widely at variance have been the views of clinicians as to the therapeutic indication in cases of bleeding as well as the lack of knowledge of drug action.

VEGETABLE AND MINERAL ASTRINGENTS.

Astringents of both classes have a distinct constricting action on tissues. They precipitate albumin and other proteids and are effective only when applied locally. The vegetable astringents owe their activity largely to their tannin content. Tannic acid is itself derived from the oak gall and seems to consist of an anhydrid combination of gallic acid (Cushny). The greater part of the tannic acid administered is decomposed in the intestine into gallic acid. Hamamelis, gallic and tannic acid are alone of interest to us in this group.

Despite the fact that these remedies are administered routinely for the control of internal hemorrhages there is no satisfactory evidence, whatever, that they are of any value. Tannic acid is found in the tissues in minute quantities as a gallate or tannate of soda and the traces are so minute that they can have no action.

The mineral astringents, notably the salts of lead and iron, are very commonly prescribed for their supposed internal hemostatic action. They are, however, valueless for this purpose, being absorbed in very minute quantities and having no predilection for the bleeding point. If they were capable of coagulating the blood after absorption and thus stopping hemorrhage they would certainly do so in the portal circulation and would not be carried to the bleeding point before they acted. . . . They never reach the blood except in forms in which they have no astringent nor styptic action (Cushny).

SUPRARENAL EXTRACT.

The local effect on the vessels of preparations of the suprarenal glands is most marked and they have the added value of not producing a rise of general blood pressure when locally applied. The extract has been used with satisfactory results in gastric hemorrhage and it may be injected into the uterus, rectum and bladder, but it is only useful where a local application can be made. There is no satisfactory testimony that the bleeding point can be reached through the circulation. Experimentally it has been determined that when a small amount of epinephrin is injected into the blood vessels of animals that there is a very rapid rise of blood pressure with a slow heart beat; further, it has a distinctly selective action, some of the vessels being affected very much more than others. In the organs whose flow of blood is regulated by the splanchnics the effect is most marked while the vessels of the lung and brain do not seem to be affected; those of the skin are much contracted, and those of the muscles scarcely influenced. The rise of blood pressure following the intravenous use of epinephrin (which is a very unstable product) would be a contraindication to its use in internal hemorrhage.

DIGITALIS.

Digitalis is sometimes prescribed to stop hemorrhage, but the flow of blood is increased through the contracted arteries and there is no evidence but that more harm than good would accrue from the administration of large doses of the drug.

ERGOT.

Ergot, on account of its selective action on the uterus, however uncertain the method of this action may be, has found an established place in the treatment of hemorrhage from this organ. The general action of ergot, which depends on its still doubtful complete composition, is not satisfactorily known. As a remedy in internal hemorrhage it may be said to be of doubtful value on account of its slow and lasting action. The rise of blood pressure which follows its use may or may not be general and may or may not affect the vessels of the bleeding area. If it is general, it would be harmful by more than counterbalancing the local contraction of the bleeding point and, further, if the vessels contracted did not include the bleeding area the rise of pressure would then be a counter-indication to its use. There is excellent reason for not using it in pulmonary hemorrhage, for pharmacologic studies have shown that it produces a distinct rise in blood pressure in the pulmonary artery.

OPIUM.

Opium, preferably in the form of morphin, is of great value in internal hemorrhage and this, not from any hemostatic action it possesses, or vasomotor effect, but because it allays the patient's restlessness and nervousness, thereby favoring clotting of the blood.

HYDRASTIS.

Preferably in the form of hydrastinin, has some reputation as an internal hemostatic, especially in menorrhoea. It is a distinct stimulant to the circulation, causing a prolonged rise of blood pressure and a slowing of the pulse after moderate dose. The cause of the increased tension is not settled; there is probably stimulation of the vasomotor center and the peripheral vessels

are contracted possibly by direct action on their walls. The drug might be used in hemorrhages of a slow, oozing character, but in no others.

IPPECAC.

The use of emetics in hemorrhages, especially pulmonary, has not met with favor of late. Graves, Trouseau, Peter, Massina, H. Weber and others were strong advocates of the use of large doses of ipecac, it being claimed that there follows a diminution in the size and strength of the pulse, and, in addition, that the blood is expelled from the bronchi where it is likely to become the source of reinfection. The great liability of the retching to induce fresh hemorrhage is a strong contraindication to its use. In tropical dysentery the drug seems to be almost a specific; we are in doubt whether this action is due to the alkaloids or the large amount of tannin the root contains.

ACONITE.

Aconite in small doses produces a slowing of the pulse with the fall of blood pressure, and seems especially indicated in the so-called sthenic cases. Aconite slows the pulse in the same way as digitalis but does not accelerate the arterial tension as does that drug.

NITROGLYCERIN AND THE NITRITES.

This group produces a profound fall in blood pressure by the dilatation of the peripheral vessels. It is stated that the vessels of the abdominal organs and the brain are more affected than those of the extremities. This group has been recommended for pulmonary hemorrhage. It would seem, however, that the general widening of the blood paths, together with the fact that the heart beats more rapidly under the lowered pressure, would contraindicate its employment. The general widening of the blood paths will frequently increase the caliber of the vessels of the bleeding area.

THE ANTIPYRETICS.

Antipyrin, especially of this group, possesses valuable properties as a local hemostatic, and has been employed internally for its supposed general syptic action. There is no evidence, however, that it possesses such. The depressant action of these drugs on the heart, together with the sedation which they often produce, may be of slight value.

FORMALDEHYD.

As a remedy by irrigation in the necrotic forms of dysentery, weak solutions of formaldehyd have been used with success. It has also been employed in climacteric hemorrhage and in uterine hemorrhages of unknown origin, by intrauterine application of a 40 per cent. solution of formaldehyd. A few drops of a very weak solution have been recommended for internal administration in gastric hemorrhage, yet the drug is distinctly toxic and highly irritating.

STRYCHNIN.

The action of this drug in producing stimulation of the vasomotor center has caused it to be employed for abdominal hemorrhage, owing to the constriction of the arteries of the abdomen and the dilatation of the vessels of the skin. Since, however, the blood pressure is raised and the drug possesses the property of producing motor excitement, it would not seem to be indicated in hemorrhage unless the patient was in a state of absolute collapse. The heart rhythm is slower after its use owing to

the stimulation of the inhibitory center, but the rise of blood pressure would seem to more than counterbalance any good this might do.

ALCOHOL.

The use of alcohol in cases of hemorrhage is generally deprecated by recent writers. As a matter of fact, the whole problem of the action of alcohol is more or less *sub judice*. We know that in fevers it will frequently slow the heart, which action is probably brought about by lessening the cerebral excitement. This action might be of distinct use in hemorrhage. The drug in therapeutic doses produces but slight fall in blood pressure. There is some widening of the blood paths, but this is not great. Taking the evidence under consideration, the employment of alcohol in cases of severe hemorrhage (shock) may rest with the personal preference of the physician. A good deal has been said on both sides.

THE PURGATIVES.

The employment of purgatives is recommended in certain forms of bleeding, as in pulmonary and cerebral hemorrhages, as a satisfactory means of lowering the blood pressure. When the need is imminent, as in certain cases of apoplexy, venesection is preferable, and it is a mooted question whether the physical and mental strain induced by purgation in general will not more than compensate any good that may follow such treatment.

SALT SOLUTION.

Isotonic salt solutions (0.6 to 0.9 per cent.) are administered with excellent immediate results when the body has lost considerable blood or other fluid. Such solutions, by whatever route administered, are absorbed rapidly and are unirritating. The rapid improvement in the circulation which follows their employment is due to the mechanical effect of the increase of fluid, but they do not stimulate the heart directly.

CALCIUM CHLORID.

Within the past ten years calcium chlorid has gained considerable reputation as an internal hemostatic, it being claimed by Silvestri, Wright and others that its administration distinctly increases the coagulability of the blood. Wright, however, emphasizes the fact that after the dose is given in full dose for a number of days, from 30 to 60 grains, thrice daily, a reverse effect is produced. G. Gross and others have used calcium chlorid in bleeding from the uterus, administering it both internally and by vaginal douche. It is a common practice among surgeons to use it routinely for a few days prior to operation on such organs as the liver and pancreas, it being claimed that this checks the hemorrhagic tendency quite effectually. The clinical evidence of its value is far greater than the pharmacologic evidence, it being urged that the coagulability of the blood can scarcely be increased by the administration of the lime salts, since more is taken in the food than is sufficient for the organism, and the chlorid is not more easily absorbed than the combination present in the food.

GELATIN.

The Chinese and Japanese have used gelatin as a hemostatic for hundreds of years, and among western clinicians it has come into general employment since its recommendation by Dastre and Floresco in 1897. The drug may be used either by mouth or rectum, or hypodermically after thorough sterilization. It is

claimed by many to possess a coagulant action on the blood, but so eminent authority as Cushny states that there is no satisfactory evidence that the clotting is accelerated by its use.

In the articles whose authors concede the hemostatic action of gelatin there is not a satisfactory explanation for the effect. Zibell believes it to be due to the lime salt contained, .6 per cent. being found. This is a very small amount to account for such action. Edsall suggests that the increase in coagulability is brought about by the more rapid formation of fibrin ferments, owing to the destruction of the red blood corpuscles. Certain oils, notably turpentine and erigeron, while possessing no distinct hemostatic qualities, may yet act beneficially by their local constricting action in certain cases, as in intestinal hemorrhage of slow oozing character.

CONCLUSIONS.

In conclusion, it is necessary to bear in mind that the direct indications for treatment vary with the individual case. These indications include the source of the hemorrhage, the condition of the circulation and the amount of blood lost. In cases of total collapse, alcohol and strychnin would probably prove of value. Fainting from loss of blood may not in itself be an indication for medical treatment, for we know the value of this condition in inducing thrombosis.

The use of the vegetable and mineral astringents in those cases in which the bleeding point can not be reached directly, is highly illogical. The same is true of the use of the mineral acids. Aconite approaches the action of this group on the circulation, without the untoward local effects.

Ergot seems distinctively harmful in pulmonary hemorrhage, and from its action can scarcely prove of any value in other than uterine bleeding.

Hydrastis has some value in similar conditions. The susceptibility of the splanchnic area to vasomotor influence might be utilized by administering hydrastis and strychnin in bleeding of this region.

I have never seen noteworthy or conclusive results follow the employment of gelatin or calcium chlorid. Normal salt solution is undoubtedly a valuable agent, and immediate response often follows its use. I have had poor success with suprarenal extract administered for its internal hemostatic effect and believe that the indications for its employment are distinctly local.

There is great reliance to be placed on rest and quiet for the patient who is bleeding, and often this will suffice. Collateral measures, ligation of the limbs, change of posture, etc., are of great service. Next in importance I should place morphin to induce quiet. In those patients whose circulation is powerful, aconite is of unquestioned value. In gastric hemorrhage, there is a great tendency to employ the astringents. It is well to mention the impossibility of their reaching the bleeding point, the stomach being filled with blood and often with partly digested food. Suprarenal extract, while at times serviceable in such conditions, may fail for the same reason. Many of the drugs advised are nauseous and should be especially avoided; emetics or drugs disturbing the stomach are only likely to cause increased bleeding, owing to the physical strain of the emesis.

This very brief and incomplete review has been presented to emphasize the fact that we have not at hand a single internal hemostatic, the value of which is generally conceded; to show further that many of the

agents employed do far more harm than good; that many are positively dangerous, and that a careful study of the individual case will generally show that very little drug treatment is indicated or can in any way do good. The physician is not certain in a particular case whether he has in any way aided nature in her efforts to check the bleeding.

The claims made for suprarenal extract, gelatin and calcium chlorid have not, in my experience, been borne out by fact.

DISCUSSION.

DR. WILLIAM J. ROBINSON, New York City, agreed with Dr. Coley that opium or morphin is of great practical value in internal hemorrhage, especially combined with a little atropin. He considers ergot unsuitable in hemorrhages from the lungs because it causes a rise in pressure in the pulmonary circulation. In gastric hemorrhage good results may be obtained from large doses of bismuth subnitrate, half an ounce at a dose. The patient should be kept in a reclining position and the stomach kept at rest. Aromatic sulphuric acid as an astringent is not safe in pulmonary hemorrhage, nor in gastric hemorrhage. In some cases of epistaxis that show great resistance to treatment, the bleeding will stop after the application of peroxid of hydrogen. Applications of fluid extract of hamamelis generally will control hemorrhage. Two hundred c.c. of gelatin injected into the back stopped a pulmonary hemorrhage which had resisted all other treatment. The patient died a few hours later and the pulmonary cavity was found filled with a large recent clot, showing the effects of the remedy. A number of cases are on record in which the use of gelatin was followed by recovery. One case of hemophilia was cured by gelatin, the treatment extending over six months. Dr. Robinson called attention to the great value of veratrum viride in hemorrhages; it does not act as an astringent; it lessens the peripheral resistance and lowers the pressure in the area around the point of hemorrhage.

DR. WILLIAM F. WAUGH, Chicago, suggested the use of atropin in addition to other therapeutic agents, as by its means the blood is directed to the peripheral vessels and can not flow from the wound at the same time. The life of a boy, with a pistol wound and apparently dying of hemorrhage, was saved by giving nitroglycerin to attract the blood to the capillaries, and atropin was given to keep it there. This was all that was needed. The action of hydrastinin is so slow as to exclude its use in all hemorrhages except those due to capillary oozing; it is not to be relied on in sudden uterine hemorrhage.

DR. W. C. ABBOTT, Chicago, emphasized the value of morphin, especially when combined with a little atropin, in pulmonary hemorrhage. Atropin relieves pressure and the morphin relieves the irritation in the respiratory organs, and quiets the patient. Therefore, the dose of morphin should be very small and that of atropin relatively large in order to produce the best effect. It is probably the fact that the arterioles around the area of hemorrhage are contracted by the effort of Nature to stop the hemorrhage. There is also a mental unrest and fear of bleeding to death, which by suggestion increases the condition. The morphin, therefore, aids the atropin in drawing the blood away from the part. The combination has no hemostatic action in typhoid fever.

DR. HORATIO C. WOOD, JR., Philadelphia, said that in a case of external or of internal hemorrhage the object of treatment is to permanently close the bleeding points with a clot. Therefore, any drug which causes increase of blood pressure does harm. The only reason that more patients are not killed by ergot is because it is used in too small doses. Atropin is equally with ergot contraindicated in hemorrhage; it elevates internal pressure more even than does ergot. Nature stops hemorrhage by lowering blood pressure until the blood has had time to clot. For this reason aconite in small doses may be useful. Stimulants may be of value, not, however, to check the bleeding, but to sustain the heart. Dr. Wood believes that

gelatin is of great value in increasing the coagulability of the blood, and pointed out that all the colloid substances possess this property. One reason why gelatin sometimes fails is because it is not used properly. In a Philadelphia hospital, a patient with typhoid fever had hemorrhage from the bowels. One-half an ounce of gelatin was ordered given every hour until relieved. The next day the same hemorrhage was going on, and it was found that a tablespoonful of ordinary prepared gelatin had been given, which contains about 3 per cent. of gelatin. Half an ounce of the dry gelatin must be given in order to have any effect.

DR. HENRY W. COOK, Richmond, Va., emphasized the danger of giving stimulants to persons with hemorrhage. A patient who was very badly injured and in shock from hemorrhage was given adrenalin, which caused a rise of blood pressure, but disturbed the clot; bleeding returned and he bled to death in ten minutes. Vasodilators may push the patient over the border line and cause death. Tentative treatment until the patient is over the danger point is the best treatment.

DR. W. B. ROBINSON agreed as to the value of gelatin in increasing the coagulability of the blood. When administered to a dog, the blood drawn will coagulate in ten minutes, while the blood from another dog, without gelatin, requires half an hour. It should be remembered, however, that the gelatin should not be cooked when given for this purpose, as by cooking it is converted into a different substance.

DR. ABBOTT disagreed with Dr. Wood, who said that atropin is not a remedy to give in internal hemorrhage. Dr. Abbott said that his views were derived from experience at the bedside. The increase of pressure at the point of hemorrhage will be overcome, if there is dilatation elsewhere, by the use of atropin.

DR. C. E. DE M. SAJOUS, Philadelphia, asked if some of the authorities quoted do not state that the action of the atropin is exercised on the arterioles. He said that this would sustain the contention of Dr. Abbott. One would have, in that case, to recognize the fact that the arteries are supplied with a muscular coat while the capillaries are not, and that the bleeding area could thus be deprived of blood and the hemorrhage arrested merely through contraction of the arterioles.

DR. HORATIO WOOD, JR., replying to questions, stated that the effect of atropin is demonstrable by placing a canula in a dog's artery. After giving atropin the blood pressure goes up, because the small arteries in the interior of the body are contracted. Atropin acts particularly on the arteries and very little on the veins; but the great danger is from arterial hemorrhage. Too small doses have no effect.

DR. ABBOTT said that while Dr. Wood gives atropin and gets internal rise of blood pressure, he claims that vasomotor influence sends the blood to the periphery and equalizes the circulation throughout the body.

DR. O. T. OSBORNE, New Haven, Conn., declared that one of the greatest dangers in internal hemorrhage is the contraction of the peripheral vessels, due to the fear of death. Atropin and morphin will produce peripheral flushing and will always help these cases.

DR. T. L. COLEY said that while morphin has no specific action in cases of internal hemorrhage, it allays the patient's restlessness, thus inducing conditions favorable to clotting. The use of bismuth in gastric hemorrhage is open to the same objection as the preparations of iron. In the presence of masses of food particles and blood clots the astringent action would, in the average case, be valueless and the mechanical effect slight. Washing out of the stomach in cases of gastric hemorrhage to remove the offending material is a step too fraught with danger to be employed with safety. The use of atropin seems to Dr. Coley to be contraindicated from its physiologic action—the rise of blood pressure which follows its administration. Clinical evidence is extremely unreliable in estimating the value of any treatment for hemorrhage. It is very difficult to calculate the extent of internal bleeding or the effect of a given drug. In a case of intestinal hemorrhage in typhoid fever several drugs may have been employed and we do not

know which of these, if any, has produced a favorable effect. The spontaneous effort of Nature must not be overlooked. A second patient may recover from severe intestinal hemorrhage without having received any drug treatment whatever.

A STUDY OF APOCYNUM CANNABINUM.*

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(Done Under a Grant from the National Academy of Sciences.)

Apocynum cannabinum, commonly known as Canadian hemp, has long been used by certain Indian tribes in the treatment of dropsies and as an antidote to snake-bite. The credit of being the first to call the attention of the medical profession to the value of this remedy appears to be due to M. L. Knapp who, in 1826, ascribed to it great value as a diuretic. In 1833 Griscom published the records of a number of cases of anasarca in which the drug had been used with marked benefit. Despite, however, several clinical reports confirming its utility, the remedy appears to have passed into comparative desuetude for a number of years, until in 1898 Dabney contributed a paper reviewing what was known of its physiologic action and describing a number of cases of various conditions of circulatory weakness from valvular lesions of the heart and of edema dependent on disease of the kidneys, which were benefited by the use of Canadian hemp. The evidence gathered from a review of the not very extensive literature on this drug, as well as from my own experiments, indicate very clearly that in *Apocynum cannabinum* we have a remedy of marked value, but which has not achieved such a prominent place among the practical therapeutic agents as it apparently deserves. It is strange how slowly the profession adopts new drugs, the evidence of whose value rests on the observations of experienced clinicians and scientific investigators, when compared with the avidity with which is taken up the products of interested pharmaceutical manufacturers, whose greatest recommendation rests on highly laudatory and widely distributed advertisements. The clinical evidence of the value of *Apocynum cannabinum* and the comparative poverty of studies of its physiologic action have made it appear worth while to study more exhaustively the effect of this substance on the animal organism, and especially on the circulation.

There are several representatives of the genus *Apocynum* indigenous to this country. It would seem, however, from the work of Griscom and Dabney that of this genus only the species of *Apocynum cannabinum* is of value in the treatment of dropsy, although some authorities ascribe similar virtues to *Apocynum androsaemifolium*. My experiments have been made with the fluid extract of *Apocynum cannabinum*.

CIRCULATION.

The changes in the circulation following the intravenous injection of moderate doses of fluid extract of apocynum consist in a marked slowing of the pulse accompanied with a rise of blood pressure. (Tables 1 and 2.) After large doses the pulse becomes exceedingly rapid, the pressure ascending as the result of the increased pulse rate still higher. (Tables 1 and 3.) There was no secondary depression of the circulation;

* Read at the Fifty-fifth Annual Session of the American Medical Association, in the Section on Pharmacology, and approved for publication by the Executive Committee: Drs. G. F. Butler, Solomon Solis-Cohen and O. T. Osborne.