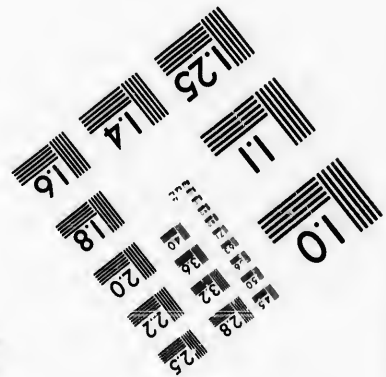
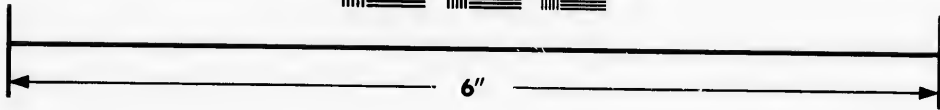
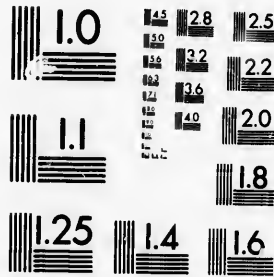


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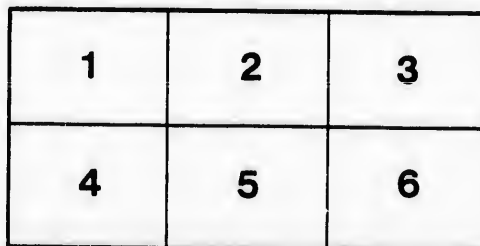
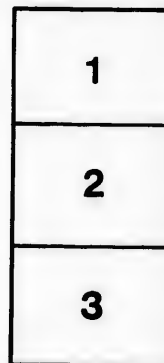
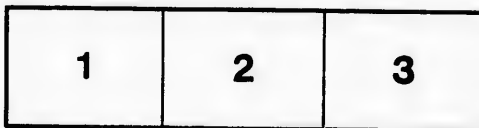
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REPORT

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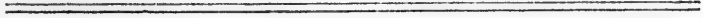
BY

JAMES STEWART, M.D., BRUCEFIELD, ONT.

Read before the Canada Medical Association at Halifax, August, 1881.



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REPORT ON THERAPEUTICS AND PHARMACOLOGY.

BY JAMES STEWART, M.D., BRUCEFIELD, ONT.

(Read before the Canada Medical Association, at Halifax, August, 1881.)

In the whole field of therapeutics, there is no subject at the present day which is so actively occupying the professional mind as that of the

ANÆSTHETICS.

Probably never since their introduction has there existed such a wide-spread desire to discover new and safer agents of this class. In regard to chloroform especially, the confidence of the profession in it is thoroughly shaken. The day of the dogmatic assertion "that pure chloroform, well administered, never kills" is past. The practical disadvantages of ether are numerous, and since its re-introduction into England there have been several instances of a fatal result from its use. Death under anæsthetics is, of course, the great and important fact connected with their use. The deaths from chloroform seem to have increased much in frequency in late years, and now amount to a very considerable number. It is very hard to estimate the exact number, as many of these cases are never published. Dr. Kappeler\* says that about 300 have been published, and Turnbull gives a list of 160 as having occurred in the 10 years between 1869 and 1879. A recent writer† says that there have been as many deaths published from chloroform as there have been months since its intro-

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\* Quoted by Reeve in *Am. Jour. Med. Science*.

† Reichert, *Amer. Jour. Med. Sc.*, July, 1881.

duction, and he considers that for every case published, two to four remain unpublished.

A very important question is, How is death caused by chloroform? If we are able truly to answer this question, we will then be placed in a position to avert it in many cases. The theories that have been advanced to account for it have been very numerous and very conflicting. The work that has been done lately in endeavouring to solve this question is of a very high scientific character, and it must be said that we have made some decided advances in this direction. Probably the work performed by the "Glasgow Committee"\* has been productive of the best results. In conducting their investigations, they endeavoured, first, to ascertain wherein the special dangers of chloroform consist; and, second, to try if some anæsthetic agent could be found which would avoid these dangers. They soon discovered that chloroform, apart altogether from its action on the respiratory centres, had a disastrous effect on the heart, while ether has no baneful influence. They now searched for an anæsthetic as powerful as chloroform, and having as little effect on the heart and respiratory system as ether. This they believe they have discovered in the ethidene dichloride. This agent was first used by Snow. He administered it in fifteen cases with good results. In 1870 it was used by Liebreich and Langenbeck. During the last year or two it has been extensively used in England. Mr. Clover† has published an account of his experience derived from 1,877 cases. In this interesting paper he gives the particulars relating to a case of death from cardiac syncope after the administration of ethidene and nitrous oxide gas, the nitrous oxide having been stopped before the ethidene was given. At the *post mortem* examination the heart was found to be enlarged, and its fibres were shown to have undergone fatty degeneration. Sauer‡ also mentions one case of death in a patient suffering from heart disease. In an extensive series of clinical investigations with chloroform and ethidene, conducted by the surgeons of the West-

\* *Brit. Med. Jour.*, Dec., 1880.

† *Brit. Med. Jour.*, May 29, 1880.

‡ *Brit. Med. Jour.*, Dec., 1880.



ern Infirmary, Glasgow, it was found that the ethidene acts quicker, but requires a larger dose than chloroform. There is a greater tendency in the case of chloroform to retardation of the heart's movements and to dicrotism. The pulse respiration ratio is apt to be more affected and oftener than with ethidene. Both chloroform and ethidene, administered to animals, have a decided effect in reducing the blood pressure, while ether has no appreciable effect of this kind. Chloroform reduces the pressure much more rapidly, and to a greater extent, than ethidene. Chloroform has sometimes an unexpected and apparently capricious effect on the heart's action, the pressure being reduced with great rapidity to almost *nil*, while the pulsations are greatly retarded, or even stopped. Ethidene was never found to produce these alarming and sudden effects on the blood pressure. The conclusion of the Committee was that the ethidene was very much safer than chloroform.

As regards comparative danger, the three anæsthetics may be arranged in the following order: Chloroform, ethidene, ether; and the ease with which the vital functions can be restored may be conversely stated, thus: the circulation is more easily re-established when its cessation is due to ether than to ethidene; and when the result of ethidene, than when chloroform has been used. The disadvantages of ether are, to a great extent, obviated by the use of ethidene, whilst the dangers of chloroform are also reduced to a minimum. Nussbaum's method of first injecting some morphia hypodermically, previous to the administration of chloroform, has lately been coming into more extensive use. It is claimed for this procedure that a much less quantity of chloroform is necessary, and that the stage of excitement, both muscular and mental, is lessened, and that thereby the dangers of anæsthesia are diminished. Mollow claims further that the morphia lessens the irritability of the air passages, and so restrains reflex action on the heart that, in this respect, its effect is similar to division of the vagus, and also that the morphia increases the blood pressure, and so is able to antagonize the deleterious influence of the chloroform for a lengthened period. Dr. Kappeler, who has had an extensive experience with this method, gives the

morphia about half an hour previous to the administration of the chloroform, and in doses of about a quarter of a grain. This mixed method, he claims, is particularly suited for nervous patients, as the narcotic allays the extreme sensibility present in these cases. Dr. Crombie,\* of Bengal, speaks very highly of this method also. For the prevention of cardiac failure from chloroform inhalation, Profs. Fraser and Schaefer† recommend the injection of atropine. Nitrite of amyl, turpentine, acupuncture and the application of boiling water to the cardiac region have all been recommended for the same object.

Another anæsthetic agent which has been attracting a good deal of attention on this side of the Atlantic lately is bromide of ethyl. First used and introduced by Nunnely, of Leeds, and lately extensively used by Drs. Turnbull and Levis, of Philadelphia. The latter says:‡ “I have used it under the most varied circumstances which could be required to test the merits of an anæsthetic, . . . . and in the most abnormal conditions of debility and shock of injury, in capital operations, through protracted periods of operations, in patients from early infancy to extreme old age.” He is convinced that it is practically the best anæsthetic known to the profession. The two leading peculiarities of bromide of ethyl are quickness of action and speedy recovery from the anæsthetic condition. Unfortunately, this agent was not long in use before two deaths occurred from its administration, one reported by Marion Sims,§ the other by Levis.|| In Sims’ case death did not take place until twenty-one hours after the operation, and therefore the fatal result was not owing to any depressant action of the anæsthetic on the heart, which is an important fact. The kidneys were found to be the seat of “Acute Catarrhal Nephritis,” and it is probable that this condition was the direct result of the anæsthetic. Several cases are reported where very alarming symptoms of cardiac failure

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\* *Practitioner*, Dec., 1880.

† *Brit. Med. Jour.*, Dec., 1880.

‡ *Amer. Jour. Med. Sc.*, July, 1880.

§ *N. Y. Med. Record*.

|| *Med. News and Abstract*, June, 1880.

have occurred during the administration of the bromide of ethyl, but where death was apparently prevented by appropriate remedies. Wood and Reichert\* have shown that the bromide of ethyl is a direct cardiac depressant, and that it at times acts out of all proportion to the dose administered. It has been asserted by Squibb† that bromide of ethyl is a loosely molecular compound, prone to undergo decomposition in the system and liberate free bromine.

Reichert,‡ in an able article, shows that it is very likely that all halogen-holding anæsthetics are loosely molecular compounds, and liable to liberate their chlorine, bromine, or iodine. If this proves to be true, we are not likely to find any safe anæsthetics in this group.

The mode of action of anæsthetics on cerebral protoplasm is a subject which has lately been attracting some attention in France. Cl. Bernard,§ in a series of experiments, demonstrated the fact that if chloroform blood is prevented from reaching the encephalon, no anæsthesia takes place. He compares the action of chloroform on the brain to a natural sleep, which is a slow anæmia of the nerve centres; but the diminution of blood does not reach lower than what is necessary for an organ in repose. He further states that the anæsthetics determine a coagulation of the substance of the cerebral cells. This coagulating action of the anæsthetics on protoplasm affects all the tissues. The heart of an animal placed in the vapour of chloroform soon loses its excitability, and when its fibres are examined by the microscope, they are found to be no longer transparent. If a nerve is submitted to the same influence, it is found to lose its transparency and excitability.

#### AGENTS WHICH REDUCE ARTERIAL TENSION.

High blood-pressure gives the earliest indications of the grave

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\* *Philad. Med. Times*, May, 1881.

† *N. Y. Med. Record*.

‡ *Am. Jour. Med. Sc.*, July, 1881.

§ H. Duret, "Les Nouveaux Anæsthetics et l'Anæsthesie," Charcot's *Archiv.*, No. 1.

series of degenerative changes throughout the body, known as chronic Bright's disease, and may, if neglected, lead to disastrous results, both in disease of the arteries and the heart. We are able to recognize this state of the circulatory system by the sphygmograph, and this instrument gives us very valuable aid in deciding what our remedies are doing. "It is very common to meet with people, apparently in good health, who have no albumen in their urine or any other sign of organic disease, but who constantly present a condition of high arterial tension when examined by the aid of the sphygmograph. Such people are very commonly subjects of the gouty diathesis, dyspeptics, suffer from functional derangements of the liver, indulge too freely in alcohol, or have, from one cause or another, tainted or impure blood." (Mahomed.)\* When this condition of the arterial system is extreme, we can feel the "persistence" of the pulse by means of the finger alone. The artery is rigid, not from any thickening of its coats, but from a constant hyperdistension. All these facts go to show that there is present a great pathological entity, and which demands the most careful treatment, if we are to prevent those changes in the heart, kidneys and other organs which will most certainly follow in the course of time. Blood-letting is probably the most expeditious method of relieving tension in cases of impending apoplexy or in the coma of uræmia.

Hamilton† speaks highly of blood-letting as *the* remedy in the initial stage of croupous pneumonia. In this disease there is high tension, but in catarrhal pneumonia we have the very opposite conditions of the circulatory system present. The reduction of blood-pressure effected by general blood-letting is not very great, and its effect is but very temporary. We have experimental proof of the truth of this shown us by Kussmaul and Tenner, who desired, after removing the whole of the cerebrum, to take successive slices off the cerebellum. They, however, found that all their normal rabbits bled to death before they could reach the conclusion of their experiments, but they found no

\* *Lancet*, August 18, 1877.

† *Practitioner*, 1880.

trouble in finishing them if they previously kept the animals on a dry diet for a period of two weeks. No deprivation of water was sufficient to bring down the blood pressure. The result of this experiment goes to show that a dry diet is superior to blood-letting as a reducer of arterial tension when we want a permanent effect. In cases of angina pectoris, due to, or accompanied by, increased arterial tension, it has long been a well-known fact that the nitrite of amyl exercises a very beneficial effect. The action of the amyl is, however, of so temporary a character that it is not adapted to those cases where we want to bring about a continuous or permanent dilatation. It has been shown by Reichert\* that the nitrite of potassium possesses this desirable property. Its physiological actions are similar in every respect to those of the amyl nitrite, but possessing a more permanent action. This action will probably be found to be of great advantage in the treatment of those chronic conditions attended by high arterial tension. Another drug which has been experimentally found and therapeutically proved to have a considerable effect in reducing systemic contraction is nitro-glycerine. Dr. Murrell† found that one or two drops of a 1 per cent solution causes a painful sensation over the whole head, which soon extends to the entire body. It causes a glow on the face, but not the great blushing we see when the nitrite of amyl is given. Nitro-glycerine gives also a similar sphygmographic tracing to the nitrite of amyl. The amplitude of the tracing is much increased; the rise and fall is abrupt. The trace displays much dirotism. Dr. Murrell has tested it in three severe cases of angina pectoris with very considerable success; a success quite equal to that afforded by nitrite of amyl. He gives 1 m of a 1 per cent solution every three hours on sugar or in a little water. Dr. Mayo Robson‡ and many others have used nitro-glycerine in angina pectoris also with beneficial results. Dr. Robson§ has also had good effects from its use in acute and chronic Bright's disease, and in the vascular tension of the aged.

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\* *Amer. Jour. Med. Sc.*, July, 1880.

† *Ringer's Therapeutics*, Ed. 7, p. 373.

‡ *Brit. Med. Jour.*, April 10, 1880.

§ *Brit. Med. Jour.*, Nov. 20, 1880.

It has also been found of marked benefit in alleviating the paroxysms of hemicrania and preventing their frequent recurrence. Cannabis Indica is another agent of undoubted value in cases of increased arterial tension. It has been shown\* that it has a remarkable influence in ameliorating and sometimes actually curing those cases of hemicrania that have for their fundamental pathological condition a contraction of the arterioles. I am not aware of its having been used in other pathological states due to or attended by increased arterial tension, but, judging from its physiological action, it would appear to be worthy of a trial. Chloral hydrat. is another drug which possesses the power of reducing arterial tension, and on this account it is highly recommended by that able physician, Dr. Fothergill, in acute endocarditis. He shows† clearly how, with rest in bed and continuous small doses of chloral, the heart is placed in the best possible condition to recuperate. By these means that increase of congestion which is accelerated by high arterial tension is prevented. He further points out the great danger of giving what is very often ordered in these cases—digitalis; for it is a well-known, but unfortunately not commonly recognized, fact that digitalis‡ contracts the arterioles and thereby increases the blood-pressure, the very condition which we should do our utmost to prevent.

This will be an appropriate place to consider the treatment of internal aneurisms by the iodide of potassium. In May of the present year Dr. Duffey,§ of Dublin, exhibited before the Medical Society of the College of Physicians in Ireland a specimen

\* The writer, in *Canada Med. & Surg. Jour.*, October, 1880.

† *Practitioner*, January, 1881.

‡ Williams, in a very important paper (*Ueber die Ursache der Blutdrucksteigerung bei der Digitalinwirkung*) published in the *Archiv. fur Exper. Path. und Pharmakologie*, Band XIV., shows that digitalis causes the following changes in the following order in the circulation:—

- (1) Increased blood-pressure with diminished pulse frequency.
- (2) Continuation of high blood-pressure with increased pulse frequency.
- (3) Irregularity of the heart when the blood-pressure is high.
- (4) Rapid sinking of the blood-pressure as the heart comes to a standstill. What is the cause of the increased blood-pressure?

§ *Brit. Med. Jour.*, June 4, 1881.

of aneurism of the thoracic aorta, which furnished an example of the disease approaching to a cure by coagulation of the blood within the sac of the aneurism, such result being fairly attributable to persistent treatment with large doses of the iodide of potassium. It is not due to irritation of the vaso-motor centre, for Böhm and Gärtz have shown that after careful cutting of the spinal cord and both vagi, digitalis will still bring about an increase, although it is not so great on account of the previous extreme dilation of the vessels. After complete paralysis of the vaso-motor centre and spinal cord by chloral, digitalis will still raise the blood pressure. Williams comes to the conclusion that the increase is due to changes effected in the elasticity of the heart's muscle by digitalis. The aneurism was not the immediate cause of the patient's death. In this case the iodide of potassium was administered in gradually increasing doses, until at last the patient was taking 40 grains three times daily. The effects of these large doses were most satisfactory. They produced no unpleasant effects. The patient obtained complete relief from the pains; the tumor diminished materially in size; it became quite firm and hard to the touch; and the pulsation in it, from being forcible, elastic and visible, was now barely perceptible; and he was discharged from hospital in this satisfactory condition, after being under treatment for four months. He died shortly afterwards from an attack of bronchitis, followed by pneumonia and collateral hyperæmia of the lungs. At the same meeting Dr. Duffey gave the details of another case that was then under his treatment by the iodide of potassium, and in which a remarkable change took place in the size of the sac; the pains were also greatly relieved. There can be no question whatever but what a few cases of internal aneurism have been cured by the iodide of potassium. For this we are indebted to Dr. Balfour, of Edinburgh. How does the iodide of potassium act? That it is not owing to the potash, as has been often suggested, appears probable from Balfour's experience, as a trial by him of other potash salts failed to have the least influence over the disease. The iodide produces diminution of the cardiac force and blood pressure, and for the production of these effects rest in the recumbent

position is not necessary. The following appears then to be the most appropriate treatment for those cases of internal aneurism that cannot be dealt with surgically:—(1) The administration of large doses of the iodide of potassium for a lengthened period; (2) Rest in the recumbent position; (3) A dry diet. Dr. Flint\* reports the case of an aneurism of the abdominal aorta, in a lady, aged 65, apparently cured by chloride of barium in doses of 2-5 of a grain continued for a period of five months.

#### ANTISEPTICS.

In this group of agents we have had lately some interesting work, a short *resumé* of which I will now give:

Klebs,† of Prague, gives an account of two cases of typhoid fever that he treated with large doses of the benzoate of magnesia. The first case, a male, aged 23, when first seen (5th day) had a temperature of  $39^{\circ}.6$ , and was in a soporose condition, and could only be aroused with difficulty. The tongue was dry and brown. He was given 10 grammes of the benzoate of magnesia during the next 24 hours, and at the end of that time it was found that the tongue was moist and the temperature down to  $38^{\circ}.1$ ; consciousness had returned. On the 14th day the temperature was normal, and remained so; the benzoate was, however, continued for 12 days longer, or, in all, for 26 days, during which time 450 grammes or 28 oz. were taken.

In the second case, a male, aged 38, the temperature on the 5th day of the disease was  $40^{\circ}.1$ . He was given daily 20 grammes of the benzoate of magnesia. Eight days after the initial shivering the temperature was normal and remained so. The patient took altogether 180 grammes of the benzoate in nine days.

Such a satisfactory result in only two cases teaches certainly but little; the result, however, is sufficient to warrant the employment of this antiseptic in still more heroic doses. There is no other antiseptic at present known that can be given in such large doses without producing disagreeable and even dangerous

\* *Practitioner*, July, 1879.

† *Arch. fur Exp. Path. und Pharma.*, Band XIV.



symptoms. If the poison of typhoid fever depends on a bacillus, as Klebs\* thinks he has proved, there is undoubtedly a great future before the antiseptic treatment of this and other kindred diseases. Jahn,† in an epidemic of typhoid fever in 1872, treated his cases with small doses of quinine, and cold baths when the temperature ran very high. He had a mortality of 23 per cent; average duration of fever 24 days. In a second epidemic (1874) he used baths alone, and had a mortality of only 8.5 per cent; average duration of fever 25 days. In a third epidemic (1875-6) he used salicylic acid, and had only a mortality of 7.1 per cent; average duration of fever 21 days. From 5i to ʒiiss of the acid or its soda salt was given daily. The use of the acid was nearly always followed by a decided reduction in the temperature, and on its being withheld the temperature quickly rose. If salicylic acid should prove to be a powerful antidote to the poisons of typhoid, we would be unable to give it in sufficient doses, owing to its producing often violent pharyngitis and irritation of the bronchi. According to both Jahn and Klebs, the salicylates have a good influence over the nervous phenomena of typhoid. Patients in a soporose condition are soon brought back to a conscious state. The unpleasant cerebral effects which salicylic acid and its salts are said to produce have not been noticed by these observers. Immerman‡ states that there were relapses in only 4 per cent of cases treated by salicylic acid, and 26 per cent of relapses in cases treated by all other means.

The antiseptic treatment of diphtheria has been attracting a good deal of attention lately. Chlorate of potash, which is used very extensively either locally or internally in diphtheria and other throat affections, is only antiseptic in dangerous doses. A saturated solution of the chlorate of potash in water is not antiseptic. It requires a strength of 1 to 5, and this is a poisonous solution; the chlorate acts as all other salts of potash do in large doses, by paralyzing the heart. As death in diphtheria frequently

\* Klebs: Der Bacillus des Abdominaltyphus und der typhöse process

† Quoted by Klebs.

‡ *Archiv. fur Exp. Path. und Pharm.*, Band XIV.

takes place in the same way, it follows that chlorate of potash is a dangerous remedy to give in doses large enough to produce any antiseptic action. Küster\* reports four cases that came under his own observation where death was in all probability brought about by the action of the chlorate of potash on the heart. Weisef recommends very highly a 2 per cent solution of salicylic acid in diphtheria. This is a strongly antiseptic solution, but not a dangerous one. He employs the following formula:—

|   |                  |       |          |
|---|------------------|-------|----------|
| ℞ | Acid Salicyl.,   | - - - | 1.09     |
|   | Sp. Vini Rectif. |       |          |
|   | Glycerine,       | - - - | āā 25.00 |

At the same time he uses benzoate of soda internally.

Oertel, ‡ of Munich, considers that he has proved that diphtheria is an infectious disease, caused by a fungus designated as "*Micrococcus Diphtheriæ*," which, localized in the mouth and pharynx, produces inflammation and fibrinous exudation of the mucous membranes and, after an undeterminable length of time, general infectious disease, the general infection being dependant upon and kept up by the local. If this theory is correct, all that is necessary is to destroy this organism, and remove from the affected parts the products of the disease. For destruction of the organism, Oertel employs carbolic acid in the form of spray (1 to 20). He has lately treated 27 severe cases in this manner, all entirely successful. The severity of these cases was such that Oertel believes that under any other form of treatment three-fourths of them would have been fatal. In the severest cases it was only after such impregnation of the blood with carbolic acid that olive-green coloration of the urine appeared that he observed a rapid diminution of the disease. For the separation and removal of the false membranes, he uses warm vapor locally, and the internal administration of jaborandi. As the latter remedy seems to be very useful in this disease, it will be more useful to mention what it is said to have done in diphtheria while on this subject.

\* *Berliner Kl. Woch.*, No. 40, 1880.

† *Berliner Kl. Woch.*, No. 4, 1881.

‡ *Arch. Laryngology*, January, 1881.

It was first used by Dr. Guttman,\* of Canstatt. He has used it for 16 months, and regards it almost as a specific. During this time he treated 75 cases—all recovered. It was given internally, and it was noticed that in a very short time it produced an active flow of saliva, by means of which the false membrane was loosened, the inflammatory irritation lessened, and the intense redness gave place to a more normal color. He uses the following formula:

|   |                      |           |        |
|---|----------------------|-----------|--------|
| R | Muriate Pilocarpine, | . . . . . | 0.02   |
|   | Pepsine,             | . . . . . | 0.05   |
|   | Acid Hydrochl.,      | . . . . . | gtt ii |
|   | Aq. Distil.,         | . . . . . | 80.00  |

Sig. One teaspoonful every hour. For adults, double the dose. Oertel† speaks very favourably of this mode of treatment. He, however, does not, like Guttman, consider it to be a specific. Lereboullet‡ reports favourably of its use. Küster§ reports four severe cases where pilocarpin acted very well; a fifth case died from nephritis after removal of the membrane from the throat. Weise|| also bears testimony to its beneficial action in a few cases; and he also adds the report of a case where he considered death was in a great measure caused by the deleterious influence of the jaborandi on the heart. It is well known that jaborandi exercises a paralyzing influence over the heart, and from late researches¶ it would seem that this cardiac influence resides in an alkaloid named jaborin, and not in the pilocarpine. Should this be true, we could get all the good influence exerted by a pure preparation of pilocarpine, and none of the disadvantages arising from other ingredients contained in jaborandi by using the former alkaloid. At present it becomes us to be very careful in ordering this drug in cases of diphtheria, and where

\* *Berl. Klin. Woch.*, No. 40, 1880.

† *Arch. Laryngology*, January, 1881.

‡ *Bulletin Général de Thérapeutique*, June, 1881.

§ *Berl. Klin. Woch.*, No. 27, 1881.

|| *Berl. Klin. Woch.*, No. 4, 1881.

¶ Ringer, *Practitioner*, January, 1881. Albertoni, Harnack and Meyer, *Arch. für Exp. Path. und Pharm.*

there are the least symptoms of cardiac failure to discontinue its administration.

While on the subject of the treatment of diphtheria, I would like to call attention to some remarkable experiments performed by Prof. Rossbach\* of Wurzburg on the action of papayotin in dissolving diphtheritic membranes. A solution of papayotin (1 to 20) dissolved a piece of croupal membrane (removed from the trachea and bronchi) into fine particles in an hour. In six hours the solution was perfectly clear, and no trace of any elements could be seen under the microscope. It took a lime solution three days to dissolve a similar membrane. In a bromine and bromide of potassium solution there was scarcely any change to be seen after four days immersion. Pepsine and weak acids affected no change after 48 hours. Owing to his supply of papayotin becoming exhausted, and no more being procurable, Prof. Rossbach was unable to put this agent to a practical test in the treatment of a case of diphtheria. He made use of another part of the plant known by the name of *succus*, but this is a very much weaker preparation than papayotin, requiring over a day to dissolve what the latter accomplishes in an hour. It was given to a child, aged 15 months, who had a diphtheritic exudation covering the pharynx and tonsils, and symptoms of stenosis of the larynx. Owing to the extensive surface involved, and weakness of the child, a very unfavourable prognosis was given. A concentrated solution of the "*Succus Caricæ Papayæ*" was pencilled on the throat every five minutes. In 24 hours the tonsils and pharynx were free from exudation. The laryngeal stenosis was, however, still present, and the local treatment was now directed to the larynx, with the result that before many hours all symptoms of the stenosis had vanished. The child, however, died from atelectasis and œdema of the lungs. On *post-mortem*, the mucous membranes of the throat and larynx were found swollen and red, but no trace of diphtheritic or croupal membrane was to be seen, except a minute patch at the anterior angle of the vocal cords. These results published by

\* *Berl. Klin. Wochenschrift*, No. 10, 1881.

such an accurate and intelligent observer as Prof. Rossbach demand the earnest attention of the profession.

The local applications of bromide of potassium, iodide of silver and fluorhydric acid have been recommended\* in diphtheria during the last year.

#### JABORANDI.

It is now several years since this drug has been employed by physicians, and although much yet remains to be discovered as to its physiological actions and uses, we are in a position to estimate in a great measure where benefit can be obtained from it. That this drug, or rather its alkaloids, are likely to come into general use as powerful therapeutic agents seems undoubted.

Harnack and Meyer† have published the results of observations which they made in Prof. Schmiedeberg's laboratory in Strasbourg on jaborandi and its alkaloids. They have found that jaborandi leaves contained not only the alkaloid pilocarpin, but also another similar body which they named *jaborin*, which was to a great extent antagonistic to pilocarpin in its action. Jaborin dilates the pupil, and has an action on the heart, salivary glands, the intestines and central nervous system exactly like atropine, and which is found also, like it, to antagonize the action of muscarine. Sidney Ringer‡ has shown that jaborandi and pilocarpin paralyze the frog's ventricle separated from the auricles, and as the ventricle contains no inhibitory ganglia, the paralyzing effect must be induced by the influence of the drug over the excito-motor ganglia or the muscular tissue, or both. In all probability the action of jaborandi on the heart is two-fold—for a heart arrested by this drug will at first contract on mechanical stimulation, but soon ceases to contract either on mechanical or electrical stimulation. As atropia antagonizes the action of jaborandi on the ventricle, it cannot act by paralyzing the inhibitory apparatus, but from its effects in the excito-motory

\* Peyrand, Gassicourt, Brame and Bergeron, in *Bulletins et Memoires de la Société de Thérapeutique*, 30 Janvier, 1881.

† *Arch. fur Exper. Path. and Pharma.*, Vol. XII., page 366.

‡ *Practitioner*, January, 1881.

ganglia and muscular substance, and he has suggested that this antagonism is due to chemical displacement.

The greatest value of pilocarpin appears to consist in its power of causing rapid elimination of effete material in cases of scarlatinal nephritis. It has been frequently administered in such cases, and with much benefit; and it appears likely that, if it be given with proper precaution, it may frequently be the means of saving life. It is frequently observed that œdema and uræmic phenomena are neither proportionate to one another nor to the quantity of urine is excreted, while in others no uræmic a normal quantity of urine is excreted, while in others no uræmic symptoms follow several days of anuria. In the former cases, the urine contains little urea; and in the latter, the urea passes from the blood into the œdemic fluid and hence becomes harmless for a time. When, however, at the beginning of convalescence, the excrementitious materials pass back into the blood, uræmia may come on, and obviously the more rapidly they pass back, the more danger there is. In virtue of its power of producing prompt and energetic increase of the sweat, salivary and other glandular secretions, pilocarpin causes a very rapid reabsorption of the transudation, and therefore its administration may give rise to uræmic phenomena, which, though transient, may be highly dangerous. There is another danger in the administration of this drug in this disease. We know that it produces a great increase in the bronchial mucus, and if the child, who is lying on his back, is too weak to cough, a catarrhal pneumonia is very apt to be induced. It therefore should be immediately stopped if there are any symptoms of pneumonia present. If pilocarpin is given with a due heed to the above precautions, it will be the means of rescuing some apparently hopeless cases of both acute and chronic nephritis.

From the observation of the fact that sufferers from prurigo feel relief when the secretion of the sweat glands is active, as, for example, in summer, O. Simon\* has been led to try the preparations of pilocarpin and jaborandi itself in this distressing

\* *Berl. Klin. Wochenschrift*, No. 49, 1879.

condition. The effects of this mode of treatment were : abatement of the accustomed sense of pruritus, softening of the skin and diminished tendency to relapse. In Hebra and Neumann's Kliniks (1879), excellent results were obtained in the treatment of prurigo by pilocarpin. Against psoriasis it was found valueless. It was found beneficial in the chronic stage, but injurious in the acute stage of an eczema. Just\* says that he has found it to act better as a pupil contracter than eserine, being free from any irritating qualities. Prokop Rokitansky† has employed the muriate of pilocarpin in uncomplicated serous pleurisy with excellent results. The effusion was quickly absorbed. The patients were kept on a dry diet.

A very marked antagonism exists between atropia and jaborandi. Atropia dilates the pupil, jaborandi contracts it ; atropia dries the skin and mouth, whilst jaborandi induces salivation and perspiration. The hypodermic injection of atropia will immediately stop the perspiration and salivation of jaborandi. A few drops of jaborandi on the frog's heart will first retard and then stop it in diastole. If a drop or two of an atropia solution be now applied, the action almost immediately recommences, and continues with unabated vigor. Falck‡ says that this is a complete physiological antagonism. From experiments performed by Ringer,§ it is obvious that pilocarpin is not the chief ingredient in jaborandi which depresses the heart, for a grain of pilocarpin only slightly weakened and slowed the ventricle. On the other hand, twenty minims of the liquid extract of jaborandi, freed from spirit, stopped the heart in ten minutes. Ringer makes the following suggestion : " Pilocarpin paralyzes the heart by combining with the molecules of the excito-motory nervous apparatus and of the muscular tissue of the heart. Atropia antagonizes pilocarpin and muscaria, because it has a stronger affinity for

\* *Berl. Klin. Wochenschrift*, No. 30, 1879.

† Loebisch und Rokitansky : *Die Neueren Arzneimittel in ihrer Anwendung und Wirkung*, S. 15.

‡ *Der Antagonismus der Gifte, Volkmann's Sammlung*, No. 159.

§ *Practitioner*, January, 1881.

the muscular and nervous structure of the heart than these substances, and displaces them, replacing their effect by its own."

#### QUEBRACHO.

First introduced by Penzoldt,\* it has been found to be a decided palliative in many cases of dyspnœa. It is especially valuable in the dyspnœa of emphysema and chronic bronchitis. In dyspnœa depending on valvular insufficiency, its value is questionable.† Penzoldt has lately experimented with an alkaloid obtained from this bark. It is called *aspidospermin*, and occurs in small, white, prismatic crystals. Ten mgrams of a 1 per cent solution of this alkaloid caused complete motor paralysis in frogs, with marked reduction of both pulse and respiration. Penzoldt administered it to eight patients suffering from dyspnœa due to various causes. In all there was considerable relief; in two this was very marked. According to Penzoldt, it has an undoubted influence over dyspnœa, especially that attending emphysema, but is inferior to the quebracho bark. Dr. Picot‡ of Carlsruhe used a tincture of the quebracho bark while doing some mountain climbing, with the result that he could climb with much greater ease and comfort. He has also used it in patients suffering from dyspnœa, and found it act well. In the same number of the *Ber. Klin. Woch.*, Berthold recommends it highly. Flint§ has used it with success also.

#### HÆMATINICS.

Since the discovery of exact methods of estimating the number of corpuscles and the quantity of hæmoglobin, we have made some advance at least in knowing how it is that some drugs, as iron, arsenic, etc., act. We are able to estimate the changes that the blood cells and their colouring matter undergo in disease, and we can tell what our therapeutic agents are doing. Hoppe-

\* *Berl. Klin. Wochenschrift*, No. 19, 1879.

† *Berl. Klin. Wochenschrift*, No. 40, 1880.

‡ *Berl. Klin. Wochenschrift*, No. 32, 1879.

§ *Medical Record*.



Seyler and Preyer have shown that one atom of iron fixes two of oxygen. The following factors have to be considered: 1. The number of red cells contained in a unit of volume. 2. Quantity of hæmoglobin contained in the same unit. 3. Individual value of the corpuscles. 4. The number of white globules. 5. The number of hematoblasts.

Of all the hæmatinics, iron still maintains, as it has always maintained, the pre-eminence as a blood restorer. There are three hypotheses as to its mode of entrance into the blood: 1. Direct entrance of iron into the blood under the form of an inorganic salt and its combination with the albuminous substances of the blood. 2. Combination of the iron and the albuminates in the stomach and intestines before absorption. 3. Absorption by these two methods combined.

E. Wild has recently shown that iron is absorbed from the stomach and intestines and then thrown out into the intestines. This explains the fact that sometimes as much iron can be found excreted through the fœces as was taken in altogether. According to Hayem\* (*De la Médication Ferrugineuse*), there are two periods in the regeneration of blood by iron. During the first the iron appears to excite the formation of the globules. Then we have new globules, containing but little hæmoglobin; the globules are more altered than when the treatment commenced. Soon these young globules become physiological, the last being the most important part of the process. When the anæmia is slight, the first phase is very short or sometimes entirely wanting, the iron in this case causing an actual decrease in the number of red cells. Cl. Bernard considered that iron only stimulated the digestive organs and never entered the general circulation at all; but this has been disproved by Hayem, who administered in two cases for a period of two months the ferrocyanide of potassium with no effect in curing the anæmia, thus showing that an insoluble iron salt is of no use in increasing the value of the individual red cells. It is the quality of the red

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\* *Bulletin Général de Thérapeutique*, p. 289, 1881.

cells that is of so much importance. Prof. Donitz\* of Japan speaks very highly of the albuminate of iron in the treatment of anæmia. He says that it can be tolerated when no other salt of iron can. It can be used hypodermically, and in this way it proved to be of great service in that disease called in India "beriberi." In this disease, hydræmia of a severe form is the most prominent pathological condition, especially in the early stages. Prof. Demarquay† of Paris has also found this salt of iron to act particularly well in cases where the other forms are not easily retained.

Next to iron, and in some forms of anæmia to be preferred to it, is *Arsenic*. It is the only drug that has been successful in the treatment of severe idiopathic anæmia. The following case recorded by Dr. Broadbent‡ is a good illustration of the value of arsenic in this disease: A woman, aged 42, who had been anæmic for four months, was admitted, and on examination she was found to have only 560,000 red cells per cubic millimètre, or 11.2 per cent. After taking 24 minims of arsenic daily for two months, the red cells had increased to 67 per cent. In the remarks appended to the report of the case, it is held "that there can be little doubt that it was a case of essential or pernicious anæmia; the patient had the appearance characteristic of this disease and the sub-febrile temperature, while the red corpuscles were not only reduced in number to an unusual degree, but deformed. Whether this diagnosis be accepted or not, the failure of iron to do good, and the rapid improvement during the administration of arsenic, are remarkable. In little more than two months the patient passed from extreme anæmia to apparently perfectly health, with wonderfully good colour of the cheeks and mucous membranes, and she continued well and strong for some months after leaving the hospital, up to the time when she ceased to present herself for examination."

Arsenic cured two cases of pernicious anæmia that were under

\* *Berl. Klin. Wochenschrift*, No. 35, 1879.

† *Medical Record*, Vol. XVI., p. 30.

‡ *Brit. Med. Jour.*, Sept. 25, 1880.

the care of Dr. Finny\* of Dublin. Whether arsenic acts in malignant lymphoma by virtue of its hæmatinic properties or not, it is a well established fact that it has proved curative in some of these cases. Several cures of this kind are reported by Billroth. Czerny has also cured cases with it. Israel† has reported the case of a woman, 65 years of age, who had a malignant lymphomatous formation infiltrating the glands of the neck, sufficient to cause difficulty in swallowing, completely cured by arsenic. The arsenic was used internally and also injected into the swelling. Lugeois, in France, for ten years has held the opinion that mercury given in small continuous doses causes an increase in the body weight in healthy persons. Keyes‡ says "that mercury in small doses is a tonic to individuals in fair health, not syphilitic. In such individuals it increases the number of red blood corpuscles." Schlesinger§ has found that rabbits and dogs taking small continuous doses of corrosive sublimate for a year thrive better than animals placed on a similar diet, but not taking the sublimate. The red corpuscles of those taking the mercury are increased more than those not taking it. Their urine showed no change in spite of the increase of the body weight. Schlesinger concludes that mercury does not increase the amount of hæmoglobin or the number of corpuscles, but that it prevents the destruction of the latter. If it increased the hæmoglobin like iron, we should have an increase in the body temperature, in the pulse, and urine solids, but the latter is shown not to be the case.

#### FUCHSINE IN BRIGHT'S DISEASE.

Prof. de Renzi|| of Genoa has used fuchsine in Bright's disease extensively. Almost after the first day there was noted a diminution in the amount of albumen in the urine and disappearance

\* *Brit. Med. Jour.*, Jan. 3 and 10, 1880.

† *Berl. Klin. Wochenschrift*, No. 52, 1880.

‡ *Amer. Jour. Med. Science*, January, 1876.

§ *Archiv. fur Exp. Path und Pharm.*, Band XIV.

|| *Berl. Klin. Woch.*, Sept. 20, 1880.

of the dropsy. The fuchsine was given in pill form 0.025 gramme twice daily. For some days the urine was coloured. In one case no result was obtained.

Dr. Brochut\* of Paris has had ten cases of albuminuria cured by fuchsine. In every case the albumen rapidly decreased in quantity, and finally entirely disappeared after a longer or shorter period. The treatment generally lasted from one to six months, and the dose of the remedy varied from 10 to 20 centigrammes ( $1\frac{1}{2}$  to  $3\frac{3}{4}$  grs.) daily.

Dr. Jas. Sawyer† has used fuchsine in many cases of albuminuria—mostly in cases of contracted kidneys,—and says that no remedy has ever given him such good results. No untoward physiological effects have been observed from its use. The mucous membrane of the digestive organs becomes deeply coloured by its use, and also the plasma of the blood. Investigation shows this latter effect to be due not to any change in the hæmoglobin, but to the solution of fuchsine in the blood.

#### HOMATROPIN.

Bertheau‡ has found that in frogs, in doses of 2 to 4 centigrammes, it causes motor paralysis, which affects all the muscles of the body, including the respiratory. Reflex action is first heightened and then decreased. Small doses have no effect on the pulse; large doses slow it, but do not cause any heart paralysis. In rabbits, small doses slow and large doses quicken the pulse. Electrical irritation of the vagus gives no constant result. This has also been observed by Rossbach. A few drops of a 1 per cent. solution causes a dilatation which lasts six hours. Dilatation of the pupils is produced by the internal administration of this drug, but it requires very large doses. It causes dryness of the mouth and throat. In man, doses of two centigrammes causes dilatation of the pupils. The pulse becomes slow; in no case was it observed to be quickened. This is quite

\* *Brit. Med. Jour.*, Oct. 11, 1879.

† *Practitioner*, January, 1881.

‡ *Berl. Klin. Wochenschrift*, No. 41, 1880.

contrary to what is seen in the experiments on animals, where we have first irritation and then paralysis of the vagus ends in the heart. Two centigrammes are not sufficient to paralyze the vagus ends in man, and large doses would be unsafe. Homatropin differs from atropine in requiring larger doses, and in its effects being much more transient. This last quality will make it valuable in many cases where temporary dilatation of the pupil is wanted.

JAMAICA DOGWOOD—(*Piscidia Erythrina.*)

This drug has recently been recommended as a substitute for opium. It is named the "fish-catching coral tree" by the natives of Jamaica. Dr. Isaac Ott\* has investigated its physiological action very fully. He finds that it is narcotic, and without any action on the irritability of the motor nerves. Its action is on the sensory ganglia of the spinal cord, and not on the extremities of the sensory nerves. It reduces the frequency of the pulse, probably by an action on the muscular structure of the heart. The arterial tension is first increased, and then soon falls. It first contracts and then dilates the pupil. In its action on a man in health, it reduces the pulse, causes salivation and sweating, disturbance of vision, itching of the skin, sleep. It has been used in cases of neuralgia with considerable success.† I have found it to act well in the semi-delirium and sleeplessness of the very aged. It has caused in a few cases alarming symptoms. When better known it will no doubt prove to be a really useful addition to our lists of narcotics. For its introduction we are indebted to the ability and enterprise of Park, Davis & Co. of Detroit.

Dujardin-Beaumetz, in presenting his work, "Leçons de Clinique Therapeutique sur le Traitement des Maladies du foie et des reins," to the Therapeutical Society of Paris, made refer-

\* Brain, January, 1881, *Archives of Medicine*, February, 1881.

† See numerous cases reported in different numbers of the *Therapeutic Gazette*.

ence\* to the remarkable power the liver possesses in destroying some alkaloids, such as nicotine, hyoscyamine, and curarine. Under some circumstances this destruction is not complete, and we find that alkaloids that have been fixed for a variable time in the hepatic tissue are thrown out into the intestines along with the bile. This action of the liver is one of great importance, and through it we can explain the innocuousness of some substances administered by the mouth, and the more powerful effects we obtain by hypodermic injections. It also is likely the explanation of the cumulative action of some drugs. We know that some agents, when given for a time, do not produce their usual physiological action, but suddenly we find this exercised in the most pronounced manner, and for an explanation of this, the peculiar action of the liver, above referred to, seems a very likely cause.

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\* *Bulletins et Memoires de la Société Thérapeutique Séance, du 23 février, 1881.*

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