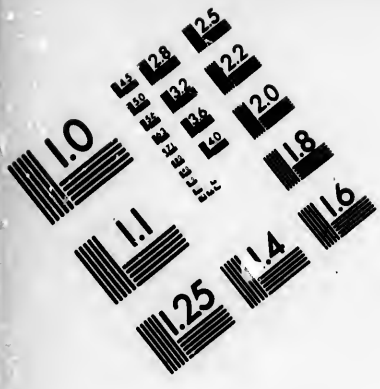

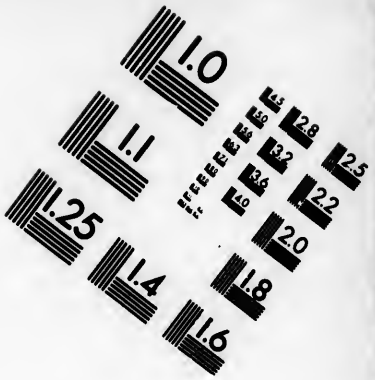

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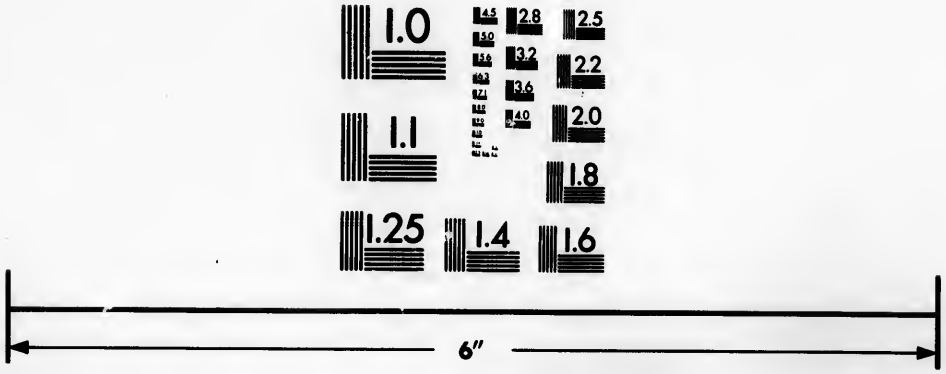

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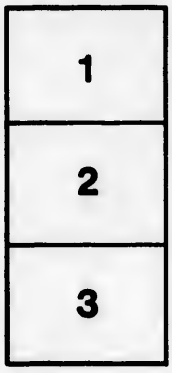

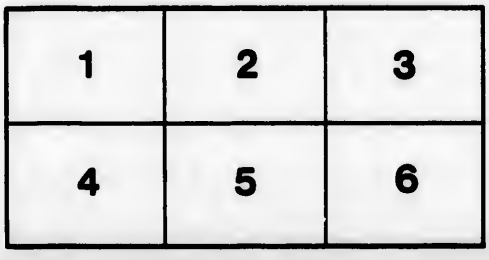

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AR. STEWART, J.

[REPRINT FROM "THE CANADIAN PRACTITIONER," TORONTO, MARCH, 1885.]

ARSENIC.

By JAMES STEWART, M.D.,

Professor of Materia Medica and Therapeutics, McGill University, Montreal; Physician to the Montreal Dispensary, and Director of the University Dispensary for Diseases of the Nervous System.

Lecture delivered before the Materia Medica Class, Feby., 1885.

ARSENIC.

Gentlemen,—Arsenic, next to iron, is our most valuable hæmatinic, but it is much more than a simple blood restorer. It possesses actions of a marked degree, which in the present state of our knowledge it is impossible adequately to explain. There is no medicinal agent, whose actions on the body are more difficult to explain than those of arsenic.

Absorption and Elimination.—Arsenious acid in all its combinations, and by whatever method it is introduced, whether by the mouth, or by the rectum, by the lungs, or by the skin, wounds or excoriations is readily absorbed and can be detected in the blood a few minutes after its administration.

It is eliminated by the skin and mucous membranes, through the bile, lungs and various glands, but mainly through the kidneys. The rapidity of its elimination varies considerably. It commences a few hours after its introduction, but it is seldom complete for a number of days. Occasionally small quantities may remain for an almost indefinite length of time, and it may

be made to reappear by the administration of iodide of potassium. It is in all probability deposited in greatest abundance in the nervous tissues. It resembles lead in this respect, but it differs from the latter that it is deposited principally in the central nervous structures, while the lead deposition is more pronounced in the peripheral nervous system.

It is supposed that arsenic displaces phosphorus in the nervous system.

PHARMACOLOGY.

1. *Its Action on Micro-organisms.*—The power that arsenic has of preventing decomposition from going on in animal tissue is well known, being made use of in the dissecting room for this purpose. Its antiseptic action, however, when brought to bear on the organisms of ordinary putrefactive material is of a very low order, being very much inferior to the more commonly used antiseptics. In ordinary medicinal doses it exerts no influence on pepsine and other non-organized ferments. After death from acute arsenical poisoning the signs of putrefaction set in about the usual time, but they speedily become arrested and the body passes into a peculiar mummified condition, in which condition it may remain for a lengthened period.

2. *When Applied Externally.*—The preparations of arsenic when applied to the skin cause

redness, inflammation or destruction of tissue according to their strength and character.

It is an irritant when applied in a mild form, and an escharotic when used in a concentrated form.

Its action as an escharotic is not brought about by any chemical influence that it exerts on the tissues. It does not, like the caustic acid and alkalies, coagulate the albuminous tissues. It acts more by direct interference with the nutrition of the tissues, causing rather a condensation and "mummifying" than an actual destruction of tissue. The escharotic action of arsenic is characterized by a high degree of inflammation, great swelling, and quick destruction of the part. It is a very painful escharotic. It should be always remembered that when weak applications of arsenic are used to destroy tissue, the arsenic may be absorbed in such quantities as to bring about fatal poisoning, while if a strong preparation is employed such a destruction of tissue takes place that absorption is prevented.

A case has come under my observation where a medical man applied a weak arsenical paste, for the removal of a malignant tumor, to the breast of a woman. It was followed by the prominent symptoms of acute arsenical poisoning, from which the woman recovered. Some days afterwards a weaker arsenical paste was used, and it was kept applied for some time.

Subacute poisoning developed, which, not being recognized, persisted, and from the effects of which the patient died some days afterwards.

The lesson to be learned from this is that in applying arsenic for its caustic action it should be used in a sufficiently concentrated form to ensure the entire destruction of the parts.

3. *The Action of Arsenic when taken Internally.*—In very small doses (0.002 to 0.004, one-thirtieth to one-fifteenth of a grain) its action is that of a gentle tonic to the gastric mucous membrane. It increases the appetite and promotes digestion. When it is given in larger doses, and yet short of quantities sufficient to produce poisonous effects, it brings about a train of marked symptoms, which will be more appropriately described under the untoward effects of the drug.

Arsenic given in small, medicinal doses has the effects of increasing the intestinal secretions and of keeping the bowels regular when there is constipation. A part of this action is probably due to the fact that it causes a transudation from the intestinal vessels.

Action on the Blood.—Arsenic enters the blood with rapidity, and, like iron, enters into combination with the red corpuscles, and not with the serum. It exists in the blood as an albuminate. Whether it has any power, like iron, of directly increasing the red cells has not been definitely determined. In all likelihood it

has no such action. The principal action of arsenic on the blood is the power it has of increasing the amount of hæmoglobin in the corpuscles. It is, in the true sense of the term, a hæmatinic. When speaking of the action of iron on impoverished blood, I mentioned that there were two distinct influences manifested by this agent—the first being an increase in the number of the red cells, the second and more important being the increase in the amount of hæmoglobin in the individual corpuscles.

The difference between the hæmatinic powers of iron and arsenic is that the former has a double, while the latter has only a single, action. Iron increases the quantity and quality of the red cells, while arsenic only increases their quality. How arsenic increases the quality of the red corpuscles is not known. It does not, like iron, supply a deficiency.

Arsenic in overdoses diminishes both the number and quality of the red cells. In this connection I will make mention of a remarkable action possessed by arseniuretted hydrogen on the red blood disks. It has the power of displacing their hæmoglobin into the blood plasma. When inhaled in excess, a sufficient number of corpuscles are destroyed so as to give rise to a condition of hæmoglobinæmia. If the coloring matter discharged is sufficient to color the urine, then we have, in addition, the condition which is now called hæmoglobinuria. Pyrogallic acid,

potassie chloride, and the different anæsthetic agents have all, when given in excess, similar actions on the coloring matter of the blood. In slight excess they cause hæmoglobinæmia; in great excess they give rise to both hæmoglobinæmia and hæmoglobinuria.

Although arsenic in overdoses interferes with the oxygen-carrying powers of the red cells, it does not destroy them.

Action on Metabolism.—Next in importance to the hæmatinic action of arsenic, and in some respects before it, is its influence on metabolism. It has a marked power in increasing metabolism. This constitutes its so-called "alterative" action. It enters into combination with living protoplasm and exercises some obscure change in it, which rests in an increase of its nutrition. The above is the action of ordinary medicinal doses of arsenic. When it is given in overdoses we find that it very seriously interferes with the complete elaboration of the changes that takes place in the albuminous tissues. It prevents the fats from undergoing their transformation into carbonic acid and water. This action is due to the oxygen carrying power of the corpuscles being interfered with. As a result, we find fatty degeneration of the muscular and epithelial structures.

In poisonous doses, arsenic, like phosphorus, diminishes the amount of glycogen; and in these doses it acts as a direct protoplasmic poison.

The influence of arsenic on nutrition is well seen in those who take it habitually, like the peasants in the Styrian Alps. These people are in the habit of taking it daily in very considerable quantities. They begin with very small doses, and gradually increase the quantity until they are able to take with impunity quantities sufficient to bring about fatal poisoning in those unaccustomed to its use. An average dose for an adult Styrian peasant is 1·00 (15 grains) of arsenious acid in the week. The arsenic-eating is commenced at an early age, and continued usually during the whole lifetime. It is claimed by these people that the arsenic makes them long-winded, and that it enables them to do an amount of work which, without it, they could not do. They increase in weight and vigour generally. They became more pugnacious and salacious.

Action on the Circulation.—When arsenic is given for some time in small doses it acts as a weak cardiac stimulant, while large doses have a depressant action on the heart. In small doses it dilates the abdominal arterioles slightly, thus causing a transudation into the intestinal canal. It is in all probability owing to this action that arsenic tends to relieve constipation. In poisonous doses it causes great dilatation of these vessels, the result being a copious serous transudation, strikingly resembling the copious rice-water stools of Asiatic cholera. It was at

one time thought that the serous diarrhœa present in arsenical poisoning was owing to the gastro-enteritis set up by its irritating action, but now we know that it is due to the paralyzing influence that it exercises on the vaso-motor fibres of the abdominal arterioles.

In poisonous doses, death is not usually caused by the depressant action on the heart, but more commonly through a paralyzing influence on the respiratory centre in the medulla. This is almost constantly the case in warm-blooded animals, while in cold-blooded animals the contrary is the rule.

Action on the Respiration.—The power that arsenic possesses of making those who take it for a lengthened period "long-winded" is probably explainable as much through its influence in increasing the hæmoglobin as through any direct stimulating influence on the respiratory centre. That the latter is a factor, however, in the production of this long-windedness is rendered probable from the experiments of Lesser.

When arsenic is given in overdoses it induces a form of dyspnœa, and in positively poisonous doses it completely paralyzes the respiratory centre.

Action on the Temperature.—When given in full medicinal doses a trifling rise in the temperature is observable. The opposite effect is constantly present from poisonous doses. This

action on the body temperature is explainable through its influence on metabolism.

Action on the Nervous System.—The action of small doses of arsenic on the nervous system is that of a tonic. This is in all probability secondary to the hæmatising influence of the drug. In larger doses, and especially in poisonous doses, it brings about a train of symptoms due to the direct deposition of the metal in the nervous tissues. It is especially apt to attack the multipolar cells of the anterior horns when given in overdoses for a long time. It produces paralysis, especially of the extensors. It resembles lead in this respect. They differ, however, in this particular, that the latter is more prone to affect the peripheral nerves, while the former is more likely to affect the central nervous system.

Remote Local Action.—During its elimination through the kidneys, arsenic does not exercise any constant effect on the quantity of urine, or of its individual ingredients. It, as already mentioned, increases, when given in small doses, the nitrogeneous waste, but it has no direct power over its elimination.

In its elimination through the skin, arsenic induces changes of a nature which are far from being perfectly understood.

TOXICOLOGY.

1. Acute Arsenical Poisoning.—The symptoms of this variety of poisoning are simply

those of a severe toxic gastro-enteritis. They come on usually half an hour after the injection of the poison, and if the dose has been large the case is almost invariably fatal. No matter how arsenic is introduced, it commonly induces a gastro-enteritis, showing that its intestinal action is for the most part not confined to the mucous membrane. After death the usual signs of violent inflammatory action in the intestinal canal are commonly discernible; but cases do occur where during life severe intestinal symptoms were present, together with marked symptoms of a nervous character, such as giddiness, delirium, pain in the limbs, paralysis and coma, and where not the slightest trace of any inflammatory action was discernible in the mucous membrane of the intestinal canal. This is the so-called "Arsenicismus Cerebro-Spinalis."

Parenchymatous and fatty degeneration of the liver, kidneys, of the epithelium of the urinary tubules, of the heart muscles and of the voluntary muscles, are constantly to be observed if the patient has lived twenty-four hours or more. Cases of chronic poisoning are not uncommon as the result of arsenical emanations from wall paper, paints, hangings, dresses, ornaments, and not only from green colors containing arsenite of copper, but also red, drab, blue, gray, and enamel papers generally, and from aniline colors fixed by arsenical mordants in carpets, curtains, etc.

The more common symptoms that result from arsenical emanations are similar to those which we find when overdoses of an arsenical preparation are given internally. They are conjunctivitis, swelling of the eyelids, sore throat, nasal catarrh, nausea, and serous diarrhœa. At times the prominent symptoms are headache, mental irritability, and restlessness. If a person has been exposed for a long time to the injurious influence of arsenic, we find, in addition to the above, paralysis of both upper and lower extremities. Arsenical paralysis is very slowly recovered from. Neuritis of the terminal branches of the radials I have observed several times in students who were engaged in dissecting. Erythematous pustules are frequently present, owing to the irritating action of the agent on the skin during its elimination. The ulcers which appear at the root of the nails are due to interference with the so-called trophic functions of the nerves. From one to two grains of arsenious acid may be looked upon as a fatal dose. In the treatment of a case of acute arsenical poisoning, after the stomach is emptied by means of the stomach pump or apomorphia, large quantities of dialyzed iron should be given repeatedly—a tablespoonful every few minutes. The freshly-prepared sesqui-oxide of iron may also be used. Neither of these antidotes are trustworthy except where the arsenical preparation has been taken in a state of solution. Your

principal aim should be to see that the stomach is thoroughly cleaned, and afterwards treat the symptomatic indications on general physiological principles. In the treatment of chronic arsenical poisoning, the source of the poisoning should be discovered and removed, and the iodide of potassium should be given internally, but not in doses of over five grains, as otherwise a sufficient quantity of the arsenic may be reintroduced into the blood to bring about acute arsenicismus.

Therapeutics.—The external uses of arsenic are unimportant. Its internal uses are, however, of very great importance. Its action for good in a number of diseases is very striking, but as to the way in which it acts in many cases, we have no positive knowledge.

I will first take up its use in the so-called blood diseases. In ordinary anæmia it is a useful agent, but much inferior to iron. It is, however, curative in some cases where iron fails to bring about more than a slight and temporary improvement. It is more efficacious in the simple anæmia of advanced adult life, than in the form that is so common in young women. Sometimes a combination of iron and arsenic is followed by better results than when either is given singly. In symptomatic anæmia arsenic is probably as powerful as a blood restorer as is iron. It is in the disease known as pernicious or idiopathic anæmia, where

the hæmatinic action of arsenic far transcends that of iron. At the present time we characterize as idiopathic or pernicious all those cases of anæmia which run a fatal course, and where during life or after death no definite cause can be found for the profound destruction of the cellular elements of the blood. Many distinguished physicians go so far as to maintain that it is not possible for a patient to recover from what is called true idiopathic anæmia, and that the fact of a case of this form of anæmia being diagnosed and cured with arsenic or any other remedy, is proof that the diagnosis was incorrect. If these views are correct, there must be a form of severe anæmia, clinically indistinguishable from the "pernicious" form, and over which arsenic has at times a curative influence.

Several cases have been recorded by the most competent observers where the use of arsenic has been followed by a complete and permanent cure where true pernicious anæmia was diagnosed.

Bramwell, of Edinburgh, gives an account of a case under his care, which was treated for a period of three weeks in hospital with full doses of quinine and iron and later with phosporized cod-liver oil. During all this time there was a steady advance in the severity of the case, and it was not checked until two minims of Fowler's solution were given thrice daily. The dose

was gradually increased until fifteen minims thrice daily were taken. The after progress of the case may be described as one of slow but uninterrupted improvement. In a month's time he was able to attend as an outpatient. Shortly afterwards he was able to go to work, and expressed himself as feeling well again. The blood from presenting the characteristic alterations of pernicious anæmia became normal. Dr. Finney, of Dublin, reports three cases of this disease, two of which made complete and permanent recoveries while taking arsenic. Dr. Campbell, of Seaforth, and Dr. Graham, of Brussels, have each had cases of pernicious anæmia under their care, where the use of arsenic was followed by complete recoveries, and where the previous use of iron had no effect whatever in staying the downward progress.

Dr. R. P. Howard, who was about the first, if not the first, on this continent to describe this disease, has had a very extensive experience of its treatment with arsenic. At the present time he has a case under observation where this agent has brought about apparently a complete recovery. The blood from presenting the characteristic alterations has assumed a normal appearance, and there is no evidence to indicate but what the recovery is a permanent one.

There is no necessity for laying before you any more proof of the value of arsenic in this disease. It is true the vast majority of cases

of this form of anæmia proceed to their fatal ending in spite of arsenic or anything else, but even in the severest forms the progress is somewhat stayed by its timely and judicious use. It should always be the first agent to receive a fair trial.

It is not known how arsenic acts in idiopathic anæmia. It is more than probable that its influence is deeper than its hæmatinic action. There is another diseased condition bearing some analogy to pernicious anæmia, where the lengthened continuous use of arsenic does good, often great and permanent good. I refer to lymphomatous formations of the lymphatic and blood glands. These formations are of a semi-malignant nature. They generally occur in young adults, and as a rule gradually progress to a fatal termination. There are a number of these cases now recorded where the internal use of arsenic and its injection into the diseased glands has brought about a permanent improvement.

Billroth has recorded a remarkable case—that of a woman, aged 40, in whom the cervical, axillary and other glands, as well as the spleen, were affected, and where the internal administration of Fowler's solution brought about a permanent cure.

Winniwater and Israel have each had cases where permanent cures have resulted. No later than a few weeks ago, a case of this

disease was shown at one of the Berlin Medical Societies, where the use of arsenic was attended by great and gradually progressive benefit.

In this connection I will mention the use of arsenic in malarial fevers. It is a well-known fact that, next to quinine and cinchonine, it is the most powerful agent we have for averting an attack of fever and ague. It appears to be especially useful in cases of long standing, where there is considerable loss of the red corpuscles of the blood, together with enlargement of the spleen.

In Diseases of the Nervous System.—Some of the most important uses of this drug are in diseases of the nervous system.

It is a valuable agent in many cases of chronic neuralgia, especially those cases depending on a depraved general state. It is said that it is of more value in facial and ovarian neuralgia than in the other more common varieties of this trouble. In gastralgia, which essentially is a neuralgic affection of the nerves of the stomach, arsenic is an agent of the greatest value.

There is one neurotic disorder where the use of arsenic accomplishes wonders, and that is in the condition called *angina pectoris*, including both the "true" and "false" varieties of this trouble.

When considering the actions and uses of the nitrites, I mentioned that they had a great

influence in relieving these attacks and also in preventing them when given in the form of a slow acting nitrite, such as the sodium nitrite. I then mentioned that these agents acted symptomatically,—that they counteracted the active pathological state present during the anginal paroxysm—the contraction of the coronary arterioles.

Arsenic, however, does not act in this manner; it appears rather to combat or prevent the actual cause of the attacks, whatever this may be. It is supposed to be nerve degeneration, but on this subject we need much light. It is not only in anginal attacks that arsenic does good, but in fact in every painful intrinsic cardiac affection. Speaking of the use of this agent in cardiac disease attended with pain, Dr. G. W. Balfour, of Edinburgh, says that "next to digitalis, arsenic is probably our most important agent in the treatment of cardiac disease; its neurotic action is undoubtedly its most remarkable one, and its effect in removing cardiac pain of an anginous character is really something marvellous." Another important use of arsenic is in the treatment of chorea. This disease is undoubtedly due to an instability of certain nervous motor centres, and it is likely that the arsenic acts here as it does in angina and in neuralgia in general. There is a general consensus of opinion that arsenic is by far the most useful agent that we have in the treatment of

chorea. In a self-limited disease like this it is necessary that great care should be exercised in drawing conclusions as to the positive value of any agent. The value of arsenic, however, is unquestionable when we find that its administration to patients who have had chorea for months and even years is followed by recovery. Numerous instances are recorded of cure from its use in cases of chorea of over two years' standing. Failure to obtain satisfactory results in the treatment of chorea with arsenic is frequently owing to a too small dose. Children of five years and upwards bear adult doses well. Girls, as a rule, require larger doses than boys. It is necessary to induce the milder physiological effects of the drugs usually before any marked difference is noticeable in the patient's condition. If these effects are brought about by small doses, the remedy should be employed hypodermically. When given in this way, doses of fifteen or twenty minims three times daily can be tolerated without the production of any of its untoward effects. In neuritis the internal use of arsenic is of much benefit. It is of especial benefit in the cases of neuritis as seen in the intercostal nerves, in the condition called *herpes zoster*. The pain preceding and following the eruption in these cases is very severe. There is no agent that can compare with arsenic in relieving this painful state. A great deal has been written about the beneficial action of arsenic in cases of

asthma of a neurotic character. I am confident that its use in this disease has been very much overrated.

In all these cases it is impossible, in the present state of pharmacology, to say how arsenic acts. In some mysterious way it exerts an influence over nervous protoplasm.

The Influence of Arsenic in Tuberculosis.— Recently renewed attention has been directed to the "anti-tuberculous" properties of arsenic by the great German surgeon, Langenbeck, who has published an account of several cases of tuberculous diseased joints where the internal administration of Fowler's solution was followed by very marked improvement both in the local conditions and general states. There is much evidence to show that arsenic has at least considerable influence in retarding the progress of the more chronic forms of pulmonary consumption. The acutely progressive cases are uninfluenced by it. The whole subject of tuberculosis, general and local, is at the present time in such a state of obscurity that it is idle work even speculating as to the possible ways that the alleged action of arsenic is brought about. Whether it is through an influence exerted on foreign protoplasmic agents in the blood, or through an influence on the metabolism of the tissues, is very far from being known.

Finally, I will refer to the use of arsenic in certain skin diseases. Not long ago, it was the

almost universal custom to prescribe this drug in nearly all cases of chronic disease of the skin. As long as cases were chronic they were considered to be fit for the arsenical treatment. There is much less of this practice since we know that the great majority of chronic diseases of the skin are curable by local means. Since the humoral element in the pathology of diseases of the skin has been practically thrown aside, arsenic is less seldom used. It is not so very long ago that physicians talked about a "herpetic diathesis," just as they talked then and now about a scrofulous diathesis, a tuberculous diathesis, an arthritic diathesis, and as alkalies, etc., are given in the latter, and iodine in the scrofulous, so arsenic was prescribed for the "herpetic diathesis." Undoubtedly arsenic has a modifying influence on a number of chronic diseases of the skin, such as psoriasis and eczema, but this influence is not due to any obscure antidotal action on the so-called diathesis, but to the fact that the arsenic influences directly the morbid changes in the skin, during its elimination. A little known but important use of arsenic is the power it possesses of preventing bromide acne, and of curing it when it is present. We are often compelled to diminish the dose of the potassium bromide, or even to stop it altogether in the treatment of epilepsy on account of the production of acne. By combining arsenic with the bromide, acne is

prevented, and much larger doses of the latter can in consequence be given. At the present time there is an epileptic attending the University clinic for diseases of the nervous system, who is enabled to take two drams of the bromide daily without its producing any rash, because with each dose of his bromide he takes five minims of Fowler's solution. Previous to the administration of the latter, half the present dose of bromide caused a disfiguring acne. A rare untoward effect of arsenic is noticeable in this case. The patient's skin has assumed since he commenced the arsenic a brownish tint. The skin of the hands and face are more deeply stained than that of any other part of the body.

This staining is of no significance. It is not caused, like the staining produced by silver, by the deposition of the metal in the tissues. It will disappear shortly after the discontinuance of the drug.

A much more common accidental effect than the staining is a general erythema ("Erythema Multiforme," or Lewin's "Dermatitis Exsudativa Erythematosa.")

This arsenical rash is well exemplified in the patient before you now, and as his case is an example of where we naturally look to the arsenic doing much good, I will give you a short account of it. He is, as you see, a powerfully-built man. He is 51 years of age. He

first consulted me five days ago, at the Montreal Dispensary, complaining of great weakness of three months' standing. His mucous membranes and face are decidedly anæmic, but owing to the diffused redness of the other parts of the body his previous general paleness is not discernible. There is a marked diminution in the numb r of his red cells. They do not exceed 3,000,000 in each c.m.m. They have not suffered much in form or in individual value, the amount of hæmoglobin being not below 80 per cent. I cannot find any gross lesion to account for this anæmia, and am therefore obliged to look upon his case as one either simple anæmia or commencing pernicious anæmia It is probably the former. When he came under observation five days ago, he was ordered 5 minims of Fowler's solution after each meal. After the sixth dose he felt feverish, and he noticed that his hands and arms were red, swollen, and very hot. The redness of the skin spread rapidly until now it involves the entire surface, except the face. On examining it closely you will find the skin covered with countless papules about the size of millet seeds. You will notice also the great œdematous infiltration there is of the forearms, the integument of which has a darker tint than that of the other parts. This is due to the venous return being hindered by the copious transudation into the subcutaneous cellular tissue.

It is very unusual to find that such a small quantity of arsenic as half a drachm, in divided doses, give rise to such an extensive and intense efflorescence as we have here. It requires no special treatment.

It would serve no useful purpose were I to simply enumerate the score of other troubles where arsenic has been or is recommended. I have given an account of its great uses; and although it is impossible to give a scientific basis for all these, I would not have you to think less of it as a power for good on this account.

It is not so many years since digitalis was given in a purely empirical manner, and we may confidently look forward to a time in the near future when we can prescribe arsenic on the same sound physiological grounds that we prescribe digitalis to-day.

Dose and Mode of Administration.—In prescribing arsenic internally, the acid itself or Fowler's solution may be employed. The latter is the favourite method of giving it; but, as a rule, it is better to prescribe it without the lavender, as the latter frequently disgusts patients. The dose varies from 3 drops up to 30 drops. In commencing the arsenical treatment of any case it is not well to give more than the minimum dose until the patient's susceptibility to its action has been determined. The dose can then, if there is no special contra-

indication, be gradually increased until 20 or more minims are taken three times daily. When it is considered advisable to give more than 20 minims three times in the day (in case of severe chorea it is sometimes necessary), it had better be given hypodermically, because this method of introduction is less liable to cause the usual untoward effects. In cases of profound anæmia, where there is irritability of the stomach, Dr. R. P. Howard has resorted to the method of giving small doses frequently and with great success. He orders a minim of Fowler's solution every hour.

When arsenious acid is prescribed, it should be given in the form of pills. The following formula, which is known as Hebra's Asiatic pills, is much employed in Germany, especially in the treatment of chronic diseases of the skin :—

℞ Acidi arseniosi..... 0·25 (4¼ gr.)
Piperis nigri..... 2·50 (40 gr.)
Mucilaginis gi. Arabici .. (q.s.)
℔. et fiat pil., No. 50.

Each pill contains 0·005 ($\frac{1}{13}$ gr.) of arsenious acid.