I would suggest that there should be: (1) an Imperial Sanitary Department attached to the Government of India; (2) a provincial sanitary department attached to each of the provincial governments; and (3) a local sanitary department attached to each municipality, district board, etc.

I have been unable within the space here at my disposal to attempt to give more than the merest indication of the mass of evidence which I have accumulated showing that water is the chief agency in the spread of cholera. With the scourge still close at our gates, let me once again urge upon every community and every responsible authority, before it is too late, to put their houses in order, and secure purity of water, of soil, of air, of habits. This is the best, the only successful, weapon wherewith to protect ourselves against cholera.

THE CROONIAN LECTURES

ON THE

PHARMACOLOGICAL ACTION AND THERAPEUTIC USES OF THE NITRITES AND ALLIED COMPOUNDS.

Delivered at the Royal College of Physicians of London.

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LECTURE II.—PHARMACOLOGY OF THE NITRITES.

Influence of Nitrites on the Nervous System.—The nitrites depress the functions of the nerve centres and nerves, but not to the extent which might be expected from their influence on the muscles, vessels, and heart. When given in toxic doses they cause in both cold- and warm-blooded animals heaviness and apathy. In man, too, cerebral depression has been seen after toxic doses. Inhalation of the vapours of nitrous ether has been followed by stupor, and after nitrite of amyl in large quantities loss of consciousness has occurred. Such effects are probably due to the direct influence of nitrites on the cerebrum.

I have never seen a narcotic influence exercised by medicinal doses of the nitrites, but drowsiness after nitro-glycerine, which acts like the nitrites, has been recorded.¹ This may be the outcome of the circulatory disturbance it causes; certainly no narcotic effect has to be feared from the use of nitrites. The sense of distension and throbbing in the head, the dizziness and the headache felt by some after amyl, ethyl, or sodium nitrites are manifestly due to circulatory changes; but the prolonged headache, which does not come on always immediately, but may last for twelve hours or more after some nitrites have been taken is probably not due to the same cause. It is most frequent after amyl and isobutyl compounds. I have felt it myself after both, and also after propyl compounds, but not after ethyl nitrite or sodium nitrite. I am inclined to think it is caused by the alcoholic radicles, and not by the nitrite element, for other amyl, isobutyl, and propyl compounds produce the same kind of long lasting headache.

Convulsions in the lower animals are rare after nitrites. They are said to have occurred in man after the injection of amyl nitrite.² I once saw twitching of the eye muscles accompany a syncopal condition which followed on the administration of nitrite of amyl. Brunton, too, alludes to the occurrence of a slight convulsive attack after the same drug. It seems likely that such attacks are connected with syncope or slight asphyxia rather than with a direct action of the drug on the brain, and considering the rarity of cerebral disturbance after any of the nitrites, and the entire absence

of fatality when they have appeared, we may, I think, safely conclude that, though the nitrites may cause some unpleasant symptoms, yet their influence on the cerebrum is no bar to their use even in full medicinal doses.

The functions of the cord as well as of the muscles are in frogs depressed by nitrites, both its reflex and conducting power being diminished, the latter, according to Atkinson, much more slowly than the former. Dr. H. Wood says that the diminution of reflex activity caused by amyl nitrite is never preceded by functional excitement. In man other symptoms so far predominate that even from toxic doses no distinct indication of an effect on the spinal cord has been noticed.

We have no proof that the motor nerves are markedly influenced by the nitrites; nor are the nerve endings especially affected by them; at least, it can be shown that they are not more powerfully depressed than are the muscles. On exposing a muscle to a solution of 1 in 1000 of sodium nitrite, and recording the contractions produced by stimulation of the muscle and nerve alternately, I find that the relative effect of the strength of stimulation is continuously maintained until the death of the muscle. (See Fig. 6.) No evidence has been given that even in toxic doses sensory paralysis is produced, or that the application of sodium nitrite paralyses the sensory nerve endings.³

To determine whether it possesses any analgesic influence other than that which arises from its effect on the circulation, I have tried it locally and generally for the relief of pain. Locally applied I have not found it possess the slightest soothing influence. I have given it internally in doses of from 3 to 5 grains for the relief of pain in various ailments, but save in the case of pains of an anginal character, in headache, and very rarely in neuralgia, I have never found it of the slightest benefit. In all cases in which it was given with relief there have been grounds for thinking that the disappearance of the pain may have been due to circulatory changes or to suggestion. It has failed to relieve pains where the other analgesics have succeeded. A few cases are indeed recorded in which the local application of nitrite of amyl and nitro-glycerine are said to have removed the pain of toothache, and many where these drugs have relieved headache and neuralgia, but such ailments are so capable of relief by vascular alterations and mental influence that we cannot, in the absence of other indications, infer from their relief that amyl nitrite has a direct analgesic influence.

General Influence on the Circulation.—I have already alluded to the action of nitrites on the contractile tissue of the vessel walls and on the heart muscle, but the general influence on the circulation requires further notice. The most important feature of this influence is the lowering of arterial tension. Dr. Brunton⁴ in 1870 showed that the lowering of tension was due to dilatation of the blood vessels, and from the fact that this dilatation occurred even after section of the cord, he came to the conclusion that the nitrites act on the muscular walls of the arterioles, influencing the muscle fibre directly, or through the local ganglia. This view was controverted by Filehne⁵ on the ground that section of the sympathetic interferes with the vascular dilatation produced by the nitrite, and by Bernheim⁶ because after arterioles are dilated by amyl nitrite, they may be made to contract by vasomotor stimulation.

The experiments of Meyer and Friedreich⁷ supported the views which Brunton had expressed; they found that when the effect of nitrite of amyl is restricted to the brain it does not bring about a fall of pressure. The dilatation of the vessels by nitrites when the brain and spinal cord have been destroyed, and in separated organs, which can only result from their influence on the vessel walls, is of course much in favour of the view that they lower tension by their action on the peripheral vessels; and Cash⁸ has advanced further evidence that the effect of nitrite in reducing tension is the result of its action on the vessels. Like Meyer and Friedreich, he finds that nitrite of amyl produces no effect on the circulation when its influence is restricted to the brain; but he has further shown that if the head of an animal be cut off from the circulation, inhalation of pure amyl nitrite causes a rapid fall of pressure, which cannot therefore be due to influence on the vasomotor centre. He also points out that

after reduction of tension by division of the splanchnic nerves, the nitrites cause a further fall of pressure.

Besides reducing the tension, the nitrites usually quicken the pulse, and this quickening is generally accompanied, if the dose be small, by such an apparent increase in force as to give the impression that a stimulant effect on the heart has been produced, for the pulse feels fuller and more distinct. Yet experimental evidence indicates that nitrites do not strengthen the actual force of the heart's beat, and that they are capable, even in comparatively small amounts, of weakening the cardiac contraction.

The question whether nitrites are, as Dr. Reichert strongly maintains, real cardiac stimulants or not is an important one, for we find nitrites recommended not only where tension is high and relief might be expected from drugs which lower it, but in syncope, heart failure from chloroform, and other conditions in which a stimulant is indicated rather than a tension reducer, and in which any drug which greatly depresses the heart might produce serious consequences.

It may be well if I state the main facts concerning the effect of nitrites on the heart which bear upon this question. As I have shown, nitrites in the isolated frog's heart cause acceleration of beat for a short time, though the contractions are rendered somewhat less powerful and afterwards slower. Atkinson employed 1 of nitrite to 10,000 of blood, and, using William's apparatus, noticed a rise in pressure for some minutes, which he attributes to a quickened action of the heart; it was followed by a slow fall and death in forty to sixty minutes.

With 1 in 20,000 the rise due to quickened action lasted ten to fifteen minutes. In no case has any actual increase in the force of the heart's contraction been observed. But the total work of the heart may be augmented by the increased rapidity of beat. We may presume that a quickening of the heart's action similar to that in frogs takes place in mammals from the direct action of the nitrite on the heart muscle, but here a further quickening is produced by the paralyzing influence which nitrite can be shown to exercise on the vagus centre. In mammals, then, as in frogs, no evidence has yet been obtained that the individual beats of the heart are strengthened by nitrites, although at first, acting more rapidly, it may do more work in a given time. But the increase in rapidity does not make up for the weakened muscular power and dilatation of the vessels, and the tension falls. Only one observer, Reichert,⁹ records a slight rise in tension after the introduction of nitrites into the circulation, and this for not more than half a minute.

If, as experiments seem to show, the effect of nitrites is only to quicken the heart's action and not to increase the force of its individual contractions, how are we to account for the markedly greater distinctness of the pulse which is so often noted after nitrites, and for the increased height in the upstroke—the so-called “percussion wave”—of the tracing which is almost invariably seen after small doses of nitrites? Probably two causes contribute to this: (1) Owing to the dilatation of the arterioles the collapse of the artery is more complete after a dose of nitrite than before it, and the difference between systole and diastole of the artery is more marked both to the finger and in the tracing. (2) The radial artery undergoes greater dilatation owing to the relaxation of its walls under nitrite influence. The pulse, therefore, becomes larger during systole, and the difference between the calibre of the artery in systole and diastole being augmented, it is felt to be more distinct and more full.

Pick many years ago suggested that arterial dilatation might in a reflex manner give rise to increased force of heart beat. If this were the case, we ought to find in the manometrical tracing taken from the carotid of a dog under the influence of a small dose of sodium nitrite that the fall in tension is accompanied by an increase in the excursions, corresponding to the individual heart beat; but this is not so, and until we have more evidence we must conclude that though the heart may do more work in a given time, the force of the cardiac contractions is not increased by nitrites.

Although we have no proof that nitrites will increase the force of the heart's beat, we have experimental evidence that

they are competent to weaken it, and faintness is occasionally complained of after nitrites. The inhalation of amyl nitrite and large doses of sodium and ethyl nitrite are capable of producing it.

On one occasion I myself suffered from a very marked syncopal attack after taking a large dose of ethyl nitrite. Whilst my tracing was being taken I suddenly felt faint, the heart beat became slow and the excursion smaller; then a prolonged intermission occurred and faintness compelled me to lie down; the slow beat continued for some minutes after the faint feeling had disappeared.

I may mention in passing a curious result which followed from publishing in the *BRITISH MEDICAL JOURNAL* a warning with regard to this effect without stating that I was myself the subject of the experiment. A year or two after the record appeared, an anonymous novel was published, purporting to show that in consequence of vivisection being allowed hospital physicians and surgeons experimented upon their patients in a horrible manner; and subsequently an appendix called “Dying Scientifically” was issued, giving the sources from which had been culled the heart-rending illustrations of the barbarity of hospital physicians and surgeons with which the novel was filled.

Lighting accidentally upon this book some time afterwards, I was amused to find that the experiment upon myself was one of the bases of the attack made on hospital physicians and surgeons. “Who,” it was asked, “were the patients on whom such experiments were tried; and where were they found if not in the.....infirmary?” And so the trial of the drug on myself was put down as proof of the dangerous experiments made by hospital doctors upon their patients. This is but another example of the way in which antivivisectionist writers get at the “facts” wherewith they try to influence the public mind.

I have never myself seen any tendency to syncope after 3-grain doses of sodium nitrite, although I have given this amount extensively. It has been known to occur after this and larger doses.

In deciding whether the nitrites can play the part of cardiac stimulants, it is well to bear in mind the resemblance and differences between their action on the circulation and that of alcohol. Both dilate the vessels. Alcohol, like the nitrites, increases the frequency and—to the finger—the force of the pulse; but though experimenters are not agreed as to whether it increases either the power of the heart's contraction or the amount of work it does, all hold that alcohol in large amounts decreases the heart's power. In these points there is considerable likeness between the action of alcohol and that of the nitrites. The difference between the two seems to be that the nitrites are far more rapid and seemingly more evanescent in their action. They quicken the beats more markedly, and dilate the vessels more quickly and completely. They far more readily depress the action of the heart. On the whole, it seems to me we must accord to nitrites in small doses a certain degree of that kind of stimulating power which we attribute to alcohol, but it is exercised much more quickly, passes away more rapidly, and is far more readily followed by decreased cardiac power than is alcohol.

There are several points of considerable practical interest to be noted with regard to the effects of nitrites on the tension and the rate of the pulse and on the regularity of the heart beat. The influence of nitrites in the relief of disease is closely associated with, if not dependent on, its tension-reducing powers. It is important, therefore, we should know how quickly the effects of the various nitrites on tension are produced, and how long we may expect them to last.

Changes in arterial tension are not often indicated by subjective phenomena, and their extent and duration can only be measured by the sphygmograph. With this instrument I have tried by means of tracings taken frequently to estimate the time at which it reaches its lowest point and its duration.

The influence of amyl nitrite on the pulse commences a few seconds after inhalation. (Fig. 17.) The tension is reduced to its lowest point in 40 to 60 seconds, and remains extremely low for 30 or 40 seconds, the pulse waves being reduced in size and sometimes irregular. Then it rises again, occasionally suddenly and in a minute and a half to two

minutes it is only a little lower in tension than it was before the inhalation. This slight lowering may continue for several minutes. Isobutyl and isopropyl nitrites when inhaled act almost like amyl nitrite.

Sir B. W. Richardson, to whom we are so much indebted for knowledge concerning amyl nitrite, has drawn attention to the fact that when amyl nitrite is taken internally its effects are much slighter, though more prolonged, than when inhaled. Instead of the tension falling at once and recovering in two minutes, it falls gradually for usually twenty to twenty-five minutes, remains low a short time, then rises to its normal height an hour to an hour and a-half after the dose has been taken. Because amyl nitrite is such a powerful agent when inhaled one drop is regarded as the proper dose, but this is a mistake; 3 to 5 minims may be required to produce about the same effect as that which follows 2 grains of sodium nitrite.

Fig. 17.—Effect of amyl nitrite when inhaled, and of amyl nitrite and nitrate when taken internally.

A small dose of sodium nitrite (2 grains) distinctly affects the pulse in two or three minutes, the point of lowest tension is usually reached in eight to forty minutes, and distinct influence on tension ceased in from one to three hours. Ethyl nitrite has much the same effect, and on the whole lasts as short a time.

I shall not here allude to the action of other metallic nitrites, since, with the exception perhaps of the strontium salt, they are unlikely to prove useful remedial agents. The combination of cobalt with potassium I once thought might prove useful, but its effects are unreliable, because its decomposition is so greatly modified by the condition of the stomach.

	Dose.	Action Commences.	Tension, Lowest.	Duration.	Rapidity of Pulse.					
					0.	10 Mins.	20 Mins.	30 Mins.	60 Mins.	120 Mins.
Sodium Nitrite	Grns.									
	2	2 Mins.	35-70	155	66	81	—	90	87	78
	2	3	8-40	170	66	74	75	75	68	63
	2	4 m. 40 Secs.	16	75	84	90	98	92	92	70
Ethyl Nitrite (2½ p. c. solution)	Drms.									
	2	3 Mins.	17-85	175	78	96	100	93	81	74
	1	1	18-30	116	66	72	—	75	69	66
	1	2	15	70	75	75	78	75	75	—
Nitro-Glycerine	Grns.									
	1	1	15-50	115	81	87	87	92	78	—
	1	3	15	80	69	75	75	—	69	—
	1	2	5-20	50	84	84	78	78	84	74
	1	1½	3	105	69	72	69	72	64	—
	1	40 Secs.	3-6	80	70	68	72	72	74	57
	1	1½ Mins.	2-45	170	72	66	63	66	60	68

The table gives a general idea of the influence on pulse tension and frequency of the two nitrites and nitro-glycerine in small doses. Four observations on each drug have been

selected from a large number to illustrate the variations which occur in their action.

I have used the term duration of action to signify the period between the time the drug is taken and the time at which the tracing first becomes normal, but this may not be the real limit of the action of nitrites on the vascular system. It is quite possible that some vessels, as for example those of the brain, may continue dilated after others have assumed their normal condition.

After the tension becomes normal it sometimes falls again slightly, and I have noticed small oscillations in tension for a short time. How long they last I do not know, for they merge gradually into those minor differences which are observed in normal pulse tracings. For practical purposes we may look on the influence of the nitrite as ended when the pulse first reaches its normal tension.

It has been suggested that after the lowering of tension by the nitrites, reaction may occur and the tension may rise above the normal. Though I have looked for such rise I have found no distinct evidence of it.

Many conditions influence the amount of fall in tension and its duration. In people with high tension pulses the fall is less in degree and duration than in those with a circulation of low tension, in those who constantly take nitrites the influence of the drug on the circulation, though not lost, is distinctly lessened.

Though people vary very much in susceptibility, I have never seen anyone entirely unaffected by such a dose as two grains of sodium nitrite or the inhalations of amyl nitrite, but when the tension is very high and sometimes during dyspnoic attacks the effect may be very slight.

The administration of 10 to 15 grains of bicarbonate of soda with the nitrite delays the appearance of decided lower tension for a few minutes (6 to 10) and seems to lengthen somewhat the time during which the drug acts.

A point of great interest in the action of the nitrites is the minuteness of the amount which will affect the circulation; one-sixteenth of a grain of nitrite of sodium produces a distinct effect on the pulse in most people.

The effect on the circulation does not increase so much as we should expect with the size of the dose. Two grains of sodium nitrite of course lower the tension more and for a longer time than ½ gr., yet the influence is not proportionate to the difference in dose. Four to 6 grains, again, lowers the tension a little more, and sometimes for half an hour longer, than 2 grains, but here again the effects are not in proportion to the increased size of dose, and they commence no earlier.

The cause of the difference between the action of any nitrite when inhaled and when taken by the mouth probably depends upon the fact that when inhaled the whole nitrite of amyl molecule comes at once in contact with the vessel walls in the systemic system. Now amyl in very small doses dilates the vessels as a nitrite does, and quite possibly the amyl molecule accentuates the action of the nitrite molecule. Cash finds that the composition and constitution of the fatty molecules has a distinct effect on the tension reducing power of the corresponding nitrite.

The quickening of the pulse after amyl nitrite is very marked, a rise from 20 to 30 beats being common. After nitrite of sodium and nitrite of ethyl in small doses, there is usually slight quickening, but it is not always present. It is very difficult, however, to estimate the influence of a drug on the rapidity of the pulse, since the frequency of the heart's action is so easily influenced by slight circumstances. A decreased frequency of the pulse is sometimes seen after nitrites, but this, with small doses at least, is never considerable. After poisonous doses, marked slowing of the heart has been in some cases noted. This may be due to the direct influence of the drug upon the heart. It will be remembered that nitrites render the beat of the isolated heart slow after first quickening it.

Irregularity of the heart's action has been observed after the administration of nitrites, and in a few cases extreme irregularity has been reported after large doses of sodium nitrite and inhalation of amyl nitrite. Using small doses of the sodium compound, I have never seen any marked irregularity result. In two or three instances out of forty or fifty in which the pulse has been watched carefully for many

hours after sodium or ethyl nitrite, slight intermission and irregularity have occurred, which had not been recorded before the nitrite was given. Slight irregularity of the pulse is common after the inhalation of amyl, isobutyl, and propyl nitrite.

On the other hand, I have met with at least four cases in which an irregular action, fairly marked before the administration of nitrites, became distinctly less or disappeared entirely when nitrites were given. I have never seen it seriously increased, and I am quite sure the irregularity of the pulse is no bar to the administration of nitrites when for other reasons they are called for. Amyl nitrite markedly dilates the vessels of the face, neck, and upper part of the chest, but evidence of its cutaneous influence is not usually seen in other parts of the body.

Flushing of the face is not common after either sodium or ethyl nitrite, yet in some cases it occurs to a slight extent, and in one exceptional case I have known a slight diffused redness over the body as well as the face follow 3 grains of sodium nitrite.

Influence on Respiration.—Amyl and alkaline nitrites in the lower animals first increase the depth and frequency of the respiratory movements, though toxic doses paralyse respiration before the heart ceases to beat. We may assume, then, that medicinal doses will tend to stimulate respiration, so far at least as the respiratory centre is concerned. The manner in which the nitrites affect the pulmonary circulation requires further consideration. To ascertain the state of the pulmonary circulation after amyl nitrite, Filehne¹⁰ made an opening in the chest wall, leaving the costal pleura, which in the rabbit is very translucent, intact. On giving nitrite of amyl he saw no congested condition of the lung, and came to the conclusion that the lung vessels are not affected by this drug. From this it would follow that the vessels of the lung are not influenced by a nitrite like those of the kidney, skin, and extremities. To determine whether this is so or not a cat was killed by chloroform, and immediately after death placed in a warm chamber; the chest was then opened, and an inflow tube fixed in the pulmonary artery, and an outflow tube in the left auricle. The inflow tube was connected with two reservoirs of blood, to one of which 1 part in 4,000 of nitrite of sodium had been added to pure blood, and the pure and nitrite blood were allowed alternately to pass through the lung tissue, the effluent blood from the pulmonary veins being measured by means of the tube placed in the left auricle. The pressure in the lungs was kept constant by attaching a tube on the trachea to a manometer and air reservoir. (Fig. 18.)

Fig. 18.—The figures at the base represent the number of minutes during which perfusion took place, those in the perpendicular line the number of c.c.'s of blood passing through the lung. The lightly-shaded squares represent the flow whilst pure blood was passing through the vessels, the dark squares whilst nitrite blood was flowing.

It will be seen from the diagram that whilst the rate of flow with normal blood was $1\frac{1}{2}$ c.c. per minute, directly sodium nitrite was introduced an increase to 7 c.c. took place. On continuing the perfusion of the nitrite a rise to 27 c.c. per minute occurred; a change to normal blood brought the flow back again to 8 c.c. The nitrite caused the colour of the lung

to change to a chocolate brown. I have repeated the experiment several times, with varied conditions as regards pressure, etc., but always with a similar result, and I think there can be no doubt that sodium nitrite influences the vessels of the lung like the other vessels of the body. Similar dilatation was produced in other experiments by introducing nitrite of amyl into the trachea. In all cases a second perfusion of the nitrite again increased the flow.

If, as we have every reason to suppose from these experiments, the administration of nitrites is followed by temporary dilatation of the vessels of the lung, the work of the right heart may be relieved by them, and it seems to me quite possible that some of the good results observed from nitrites in dyspnoic attacks may be the direct result of the relief thus given to the smaller circulation.

Digestive Organs.—The effect of nitrites on the digestive organs varies greatly in different individuals, usually after the ingestion of sodium or ethyl nitrite slight eructations of nitrous gas occur. To some, nitrites act as powerful gastric irritants, the smallest quantity causing sickness and diarrhoea. It is easy to understand the cause of stomach irritation when nitrites are taken by the mouth, for nitrous acid is always at once set free, and to some it acts as an irritant, though most people tolerate it in small quantities, and feel no discomfort from its temporary presence. Where even inhalation causes stomach irritation and diarrhoea it is probably due to excretion of nitrites by the gastro-intestinal tract.

Urinary Organs.—From the dilatation of the kidney vessels which nitrites cause we should naturally expect that increase in urinary secretions would follow their use, and doubtless such increase does at times occur. Murrell has seen, after the administration of nitro-glycerine (which acts like a nitrite) to a patient with epispadias, an immediate increase in the flow from the ureter, and nitrous ether has long had the repute of being a diuretic; nevertheless, neither in animals nor men can it be shown that any of the nitrites continuously or greatly influence the urine flow.

In some careful experiments made on animals Atkinson found that small doses of nitrite of sodium either do not affect the urine at all, or sometimes slightly diminish, sometimes slightly increase it, but large doses always decrease it. The urea and uric acid secretion were practically unaffected. In a series of cases I have tried to ascertain the influence of continuous doses of the nitrite of sodium on the kidneys in man.

In twelve non-febrile cases free from cardiac and kidney disease I noted the influence of 3 grains of sodium nitrite given three times daily on the excretion of water during one week, and compared it with the amount excreted in the week immediately preceding and the week immediately following the exhibition of the nitrite. Seven passed more when the nitrite was given, five rather less. In only one was the increase very distinct; here it amounted to 9 ounces per diem, and, as in the week following the nitrites the increased flow was in part maintained, it is not quite certain whether the nitrites were altogether responsible for it. In a second case there was a distinct but not very great augmentation, averaging 5 ounces daily, which was not maintained when the nitrites were stopped. In all the other cases the difference between the quantity passed before and during the administration of the nitrite was too slight to suggest that any influence was exercised by it. In three cases the amount passed the day following the nitrite was distinctly increased. In these two, and a third perhaps where the increase was distinct though less marked, it is probable a temporary effect was produced by nitrites, and I believe that under some conditions nitrites do increase for a short time the secretion of water.

The estimation of urea is open to many fallacies, unless every circumstance is taken into account. I have determined the amount in many cases, and compared the amount passed whilst nitrites were being taken with the amount passed before and afterwards, and the general result I have arrived at is that nitrites do not increase the excretion of urea.

A drug which in a state of health has but little influence on the urine flow may prove a diuretic in certain conditions of disease, but I have been unable to satisfy myself

that nitrite of sodium or ethyl can be relied on to act on the kidneys in the ailments for which diuretics are needed.

In some forms of chronic Bright's disease I have seen a considerable increase in the urine follow the administration of sodium nitrite and nitro-glycerine, yet it has never been prolonged. In cardiac dropsy I have not seen continuous diuresis produced.

Notwithstanding that I hold the nitrites in light esteem as diuretics, it is quite likely that a full dose of spirit of nitrous ether has at times a distinct effect in causing a temporary increased urine flow. Half an ounce of spirit of nitrous ether represents, perhaps, the same quantity of rectified spirit and a fair dose of ethyl nitrite. Such a compound is well adapted to act both on skin and kidneys. But I have great doubt whether the administration of spirit of nitrous ether in doses of 15 to 20 minims three times daily as a mixture can be of any service as a diuretic. Even at first the amount of nitrite present is probably too small to influence the circulation sufficiently, and the dissipation of the ethyl nitrite commences as soon as the mixture is made up. One advantage the nitrites certainly have—they do not irritate the kidney.

In the lower animals they have been found capable of producing glycosuria when inhaled or injected, and even in man such an effect is not unknown. Dr. Maragliano¹, who caused his patients to inhale forty drops of amyl nitrite for forty minutes four to six times daily for the cure of epilepsy, says he found sugar in the urine in most cases.

Temperature.—The influence of nitrites on temperature is not an important consideration in their therapeutic use. The quantity in which they are given medicinally is not likely to affect tissue change, but dilating the vessels as they do they at first slightly raise the external temperature. As they expose more blood to the surface they will tend subsequently to lower the body temperature, but the effect in either direction is inconsiderable unless toxic doses are given, which very greatly reduce temperature, perhaps by diminishing oxidation.

Perspiration.—For several centuries spirit of nitre has been a popular diaphoretic, and of its effects and influence in causing perspiration under some conditions there can be no doubt. After drachm doses of $2\frac{1}{2}$ per cent. solution of ethyl nitrite in alcohol I have not infrequently seen in ten to twenty minutes the face bedewed with moisture. In this condition general perspiration has been readily brought on by the application of warmth. The same result has often followed 2 grains of sodium nitrite; in one subject perspiration usually occurred after small doses of any nitrite, even though he was not in bed. As a rule, however, no perspiration is produced by ethyl or sodium nitrites unless in conditions favourable for its occurrence. The diaphoresis is doubtless due to the dilatation of the cutaneous vessels which the nitrites cause, and is therefore but a passing effect. The value of the time-honoured cup of hot gruel, followed by half an ounce of spirit of nitrous ether, it is easy to understand; diaphoresis may result, but the diaphoretic value of 10 to 20 minims of spirit of nitre as usually given medicinally is very problematical.

Summary of Influence on Tissues.—The chief pharmacological characteristic of the nitrites is their power of temporarily affecting muscle tissue. Under ordinary conditions the amount of nitrite present in the tissues of the living body is not sufficient to disturb the functions of voluntary muscles, even though it has been shown that in solutions of 1-5,000 a marked effect on muscle. But the involuntary muscles and heart are affected by marvellously small quantities of the nitrites; whilst, however, their contractile power is impaired by these small amounts they are not really injured, for on removal or destruction of the nitrite molecules they rapidly resume their normal function, and no trace is left of their effects. If frequently exposed to these same molecules they seem to become less readily affected by them.

The tissues of the nervous centres seem to be less easily affected than the muscle tissue, but probably the influence of nitrites is here equally fleeting. Considering the very powerful action of nitrites on muscle tissue, their effects on other structures is very slight. In dilute solutions nitrite of sodium is not a tissue irritant, and is not very destructive to

the lower forms of life. Solutions of 2 per cent. and upwards applied to mucous or raw surfaces or injected under the skin give rise to pain, but the same effect is produced by chloride of sodium solutions of the same strength.

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(To be continued).

A CASE OF CÆSAREAN SECTION.

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It will be seen from the account of the following case that the extraction of a living child through the anterior wall of the uterus may be one of the most simple of operative procedures, unless the placenta be attached in front; in which case it is best to cut right through it without wasting time.

I was asked by Dr. Wilson to go to Leytonstone on March 11th, prepared to perform the Cæsarean operation, if, on consultation, we considered it to be necessary, on a patient 32 years of age. She had been married four years, and a year after marriage had been delivered of a small female child, after a long and difficult instrumental labour. There was a fracture of the skull, and the child, though completely paralysed on one side, lived for five weeks; a soft swelling on the side of the head becoming somewhat smaller shortly before death. The patient was a little, squat woman; the abdomen was large, with a comparatively small amount of liquor amnii, and the head was found to be lying in the common occipito-anterior position. It was calculated that the patient had completed at least thirty-seven weeks of gestation. On vaginal examination the os was found to admit one finger easily; the available conjugate was under 3 inches, probably little more than $2\frac{3}{4}$; the lateral space was diminished, and the descending rami of the pubes were fixed at a very acute angle. The parents were extremely anxious to have a living child. Dr. Wilson and I were agreed that it was useless to hope that the child could be born alive, and we were of opinion that the question to be decided was whether we should remove the child then, or wait and divide the symphysis pubis when labour had commenced. The points in favour of the former procedure were: the conjugate was almost outside the limit which is placed for the performance of a successful symphysiotomy, and was farther reduced by the exaggerated masculine pubic arch; and the difficulty of getting out to the country, perhaps during the night, had also to be considered. In addition, there was the advantage to the patient that the possibility of future impregnations could be avoided during the performance of the section. The matter being left entirely to us, we decided to remove the child by the Cæsarean operation rather than to delay.

It is futile to give exact directions as to the position of the incision through the abdominal wall; it must be made entirely in regard to the situation and size of the uterus, bearing in mind that the section of that organ is to extend downwards from close to the fundus. The external incision may therefore be situated partly above and partly below the umbilicus, or even wholly above; it will extend to from 4 to 6 inches, depending on the thickness of the abdominal wall. The umbilicus does not require to be avoided; the incision ought to be carried right through it, and it conduces to the exact stitching of the wound if one or two scores are made across the line of the incision with an aniline or nitrate of silver pencil. The peritoneum having been opened to the full extent of the wound, it is then necessary to be quite