hydrogen or some other sulphide, we might assume that nitric acid must be liberated at the same time. This is rendered highly probable by the fact that cultures that are alkaline before addition of bismuth subnitrate become acid after some time. However this acidity is not due to free nitric acid, but to some organic acid which the liberated nitric acid sets free from the culture medium.

However, to obtain some positive proof for the assumption the following experiment was performed. Bismuth subnitrate, when shaken up with boiled distilled water, gives a neutral reaction for about five minutes, after that it changes to acid. Ultimately it becomes so markedly acid that Congo red paper shows the presence of free nitric acid. Heat favours the reaction. This reaction gives a satisfactory explanation of the phenomena described above.

Why those flasks to which both drugs were added should not be sterilised earlier than those to which bismuth subnitrate was added alone is rather difficult to account for. A possible explanation is that the liberation of nitric acid is either delayed or retarded in the presence of β naphthol.

In the foregoing we have tried to state the facts as concisely as possible, and have avoided drawing any conclusions from them.

ON THE DIGITALIS GROUP AND THEIR USE IN THE TREATMENT OF DISEASE OF THE HEART.¹

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THE digitalis group comprises a considerable number of plants of different botanical families and of varying activities, ranging from the deadly upas to the comparatively innocuous convallaria and adonis, all of which have an action on the heart more or less resembling that of the plant which gives its name to the group.

The fundamental action of the members of this group is to increase the elasticity of muscular fibre so that it expands more slowly and contracts more perfectly. The effect of this upon a hollow muscle like the heart is that it dilates more slowly and empties itself more completely; residual accumulation is thus prevented and any dilating influences are counteracted. The heart is affected earlier and more powerfully than the other muscles because the blood passes so frequently through it that it receives a larger dose of the drug within the same space of time. For a similar reason the muscular coat of the arterioles also gets a disproportionate share of the drug and is early and strongly affected, though not nearly to the same extent as the heart, as the arterioles are only stimulated by the comparatively small quantity of blood passing to their own district. The more perfect contraction of the heart throws a larger blood wave into the arteries, and as the effect of the increased elasticity of the muscular coat of the arterioles is to keep their calibre contracted, the blood escapes more slowly into the veins, it accumulates within the arteries and the blood pressure within them is raised. The effect of this is that every muscle in the body, and amongst them the myocardium, is flushed with blood at an increased pressure and their nutrition and energy are improved and augmented by a more perfect metabolism.

The action just described is that of digitalis itself; it seems probable that, besides the general action on the muscles, each of the members of this group has a common action on the heart, coupled with specific differences of its own. We know, for example, that digitalis acts powerfully on the heart and arteries, and less so on the uterus and bladder; and that ergot acts energetically on the uterus and bladder, and less so on the heart and arteries; and Professor Fraser tells us that strophanthus acts powerfully on the heart, and but slightly on the muscular fibres of the arterioles. Fraser claims this as an advantage in favour of strophanthus; it seems to be a very doubtful advantage, and it distinctly shows that the action of strophanthus specifically differs from that of digitalis. From the absence of any marked constriction of the arterioles, any rise in the blood pressure follow-

ing the use of strophanthus must be due to ventricular action only; it is not, therefore, persistent, and can only feebly affect the muscular metabolism. We need not, therefore, wonder that when the action of the drug is withdrawn the heart is not found to have received permanent benefit, but remains pretty much as it was. Strophanthus forces on the ventricles an increase in the strength and duration of the systole, which ceases with the action of the drug. It acts as a cardiac poison and not as a cardiac tonic. In cases of valvular lesion with ruptured compensation and dropsy, strophanthus acts doubtless as a diuretic, but in this respect it is uncertain. Apart from the experience of myself and others, the very discrepancy in the dose prescribed indicates this, for while some find 5 minims of the tincture every four hours amply sufficient, others find as much as 10 or more minims every two hours to be required. Past history and present experience alike teach us that to restore a ruptured compensation in cases of valvular lesion drugs are not always required. If such a patient is put to bed, the recumbent posture at once reduces the work of the heart by ten or twelve beats per minute, and this, coupled with warmth and good food, is sufficient to rehabilitate the hearts of most hospital patients, to raise their blood pressure, increase the flow of urine, and drain their cavities. The addition of a few doses of strophanthus will not prevent this improvement, even if it does not materially assist it.

Strophanthin has, however, two advantages over digitalin; it is readily soluble in water, and it is rapidly absorbed; it is thus available for hypodermic injection, and, as it acts with great rapidity, it may be of service when administration of any drug by the mouth would be of little use. There may thus be circumstances in which strophanthin is to be preferred to digitalin, though it may be doubtful whether the hypodermic injection of ether is not more likely to be more useful than either, when the failing heart stands in need of an immediate fillip.

Strophanthus is the only member of this group which has any pretensions to rival digitalis, yet it is so much more uncertain in its action, and so devoid of tonic properties, that we are not tempted to displace in its favour our own indigenous drug.

Dotted all over our upland pastures there is no nobler plant in our indigenous flora than the digitalis purpurea, and there is no more potent benefactor to mankind among the many constituents of our materia medica. For more than a hundred years digitalis has been known as a sovereign remedy for dropsy, but it is only within the last twenty years that its true properties have begun to be recognised. And even yet the profession are hampered in its use by the continued prevalence of the idea that digitalis is a most powerful but dangerous sedative to the heart—an idea that dates from those not so far back days when digitalis was supposed to possess a number of distinct actions, all more or less antagonistic to one another. Now we know that digitalis is a tonic to the muscular fibre, and that it acts chiefly on the heart and on the muscular coat of the arterioles. From this action flow all the benefits we obtain from this drug, while any unpleasantness that may happen to follow its employment is due to the effects of an overdose, and for this the prescriber is to blame and not the drug.

Digitalis in every form is absorbed with difficulty and only slowly excreted, hence if the dose is repeated at too short an interval the drug accumulates within the system, and ere long symptoms of poisoning appear. This faculty of accumulation digitalis shares with many other drugs. Unfortunately for its own reputation its sphere of usefulness lies among a class of cases in which sudden death is no uncommon occurrence, and for many a day any sudden death in a patient taking digitalis was always ascribed to the cumulative action of the drug quite irrespective of the dose administered. Even yet there is an idea of danger connected with this drug which hinders the usefulness of this invaluable remedy. Deaths from digitalis poisoning in those otherwise healthy are amongst the rarest of occurrences; only a very few are on record. A full account of one has been published in which 211 grains of the powdered leaves were taken within five weeks before the fatal result.² Sickness, diarrhoea, faintness, and slow pulse had prevailed during fully four of these

¹ Read in the Section of Pharmacology and Therapeutics at the Annual Meeting of the British Medical Association, held in London, July-August, 1895.

² Köhnhorn, *Vierteljahrsschrift für gerichtliche Medizin*, 1876, S. 278.

weeks. Using ordinary medicinal doses with reasonable care we need have no apprehension, and in all my experience of many years I have never seen any unpleasant result follow even a somewhat free use of digitalis. As may be readily supposed, saturation is more easily brought about in small and anæmic individuals than in those who are more bulky and plethoric.

A tonic dose fitted to improve the nutrition and increase the energy of a feeble heart must always be a moderate one, and only repeated after the lapse of an interval sufficient to permit the preceding dose to be wholly excreted. In this way we secure that at the end of the interval there is a slight increase of the cardiac tone and energy, no digitalis remaining within the system. A usual and efficient dose to secure this end is 1 gr. of the powdered leaves, or an equivalent of any of the other preparations of the drug, every twelve hours. Such a dose may be continued safely for so long as may be required without risk of saturation. The feeble heart slowly and steadily improves, an imperceptible impulse becomes perceptible, and a feeble impulse a strong one, the patient meanwhile slowly acquiring an increasing sense of well being and capacity for exertion. Such a tonic dose may be safely continued for years with nothing but increasing benefit to the patient, and without the slightest need for any anxiety as to the possible occurrence of any disturbing saturation.

When we wish to contract young hearts which have got dilated, or to excite diuresis, we must employ larger doses than such as are merely tonic, and as these larger doses have a cumulative effect the patient taking them requires a little more attention.

The young dilated hearts we wish to contract are either such as follow various febrile affections occurring in early youth, or are the flabby dilated hearts of those who are chlorotic or anæmic. Such heart affections are often called functional, and the sufferers are supposed to grow out of them. But it is distressing to find a few years later that a want of timely attention has left this so-called functional affection as an obstacle to entering a profession or a hindrance to making provision for a family.

When the heart is feeble and dilated it beats more quickly and less forcibly than in health, the ventricles empty themselves less completely, there is residual accumulation within their cavities, the arteries get depleted and the veins over-filled. The result of this venous stasis is a soakage of all the tissues, and by persistence of all the conditions this ultimately collects as dropsy in the more dependent parts of the body and within its cavities. This dropsical accumulation is chiefly of consequence as an indication of heart failure, but in the tissue interspaces, and especially in the extremities, it constitutes an important peripheral obstruction to the circulation, increasing the work of an already failing heart.

In such cases our forefathers employed digitalis empirically as a diuretic, often with a dangerous freedom, sometimes giving as much as from 10 to 20 gr. in powder or infusion every hour or every two hours till nausea or sickness occurred. This sickness was accompanied by great diminution or complete suppression of urine, and was followed in two or three days by copious diuresis. Nowadays we know that digitalis has little if any action on the kidneys, and that it produces diuresis by improving the condition of the heart and circulation. As the arteries fill and the veins empty the effusion is absorbed, the blood gets more watery, and this excess of water is excreted by the kidneys. We need not, therefore, run any risk by giving absurdly large doses; a simple tonic dose acts as a diuretic by maintaining the integrity of the circulation; but when the heart is dilated as well as feeble and the accumulation of fluid considerable, we require to act a little more energetically. A moderate dose is, however, quite sufficient; 3 gr. of digitalis, either in powder or infusion, every eight hours, will be found a very efficient diuretic. Only exceptionally will a larger dose be required, and we must always remember that the larger the dose and the shorter the interval between the doses the more watchful we must be for symptoms of saturation. These symptoms may be looked for as soon as 30 to 40 gr. of the drug have been ingested; they are—diminution of a primary diuresis, slowing of the pulse, or nausea, more rarely diarrhoea. If the medicine is stopped on the first occurrence of one or other of these symptoms, the patient

will suffer no damage, nor will the physician ever be disappointed in any reasonable expectation. This is Withering's statement, and with him I entirely agree. When symptoms of saturation occur diuresis diminishes, and almost complete suppression may last for two or three days; diuresis then recurs and may continue till all the fluid is drained off, or it may be readily kept up by a moderate dose at regular intervals of eight to twelve hours. Apart from any diuretic action, these cumulative doses, by gradually improving the tone and elasticity of the myocardium, not only enable it to resist dilating influences, but in favourable circumstances are able to restore a dilated heart to its normal dimensions.

Much larger doses than those indicated are frequently given without detriment. It is on record that a young woman affected with mitral stenosis took for six years $4\frac{1}{2}$ gr. of digitalis leaves in infusion night and morning, with nothing but continuous benefit. Without her medicine she was unable to work, her limbs were cedematous, flashes of light dazzled her eyes, a rushing sound disturbed her hearing, her heart felt full to bursting, and her urine was suppressed. All these symptoms disappeared within a few hours after her medicine was repeated, and she was once more an active woman.² But such a case must be exceptional, and so large a dose cannot be recommended.

The first effect of a moderate but cumulative dose of digitalis is slight slowing of the pulse, with increased tension, and a gradually increasing flow of urine. After the ingestion of about 30 gr. we look out for signs of saturation; with moderate doses there are a more marked slowing of the pulse, and a diminution in the flow of the urine, immediately followed by a tendency to cardiac irregularity, the slow heart beat quickens, falters, and intermits on the slightest exertion. Unless we remember that after the administration of 30 gr. of digitalis we approach the point of saturation and are watchful, a slight drop in the pulse-rate, or in the quantity of urine is apt to pass unnoticed, and the patient may get plunged into all the discomforts incident to vagus paralysis, while we are scarcely aware that the drug has begun to affect him. This, however, is not the fault of the drug, but an error on the part of the practitioner.

The slow pulse of digitalis action seems quite devoid of danger, but the rapid irregular pulse of digitalis poisoning certainly indicates a condition that is not free from risk, though it may be safely tided over by strict adherence to the recumbent posture and the moderate use of stimulants.

It is well to remember that after symptoms of saturation have appeared, the full diuretic effect of digitalis is often displayed for two or three days. The remembrance of this may help to prevent needless dissatisfaction with the action of the remedy, and in some cases it may avert the ascription of this postponed action to some much less effective drug. Now and then we meet with a constitution so sensitive to the action of digitalis that symptoms of saturation follow the ingestion of less than half the usual quantity, such cases are rare, and when met with must be treated on ordinary principles, with the necessary limitation of the maximum dose.

Digitalis may be beneficially employed in all cases of heart failure whatever may be the cause or the nature of the concomitant lesion. In cases of valvular lesion, apparently fully compensated, digitalis may not be imperatively called for, but as in all such cases heart failure is steadily if slowly progressive, no harm can ever result from giving tonic doses of the remedy sufficient to maintain the normal elasticity of the myocardium. Some object to this, especially in certain forms of valvular lesion, from an idea that "the heart may be thus unduly stimulated, and the left ventricle hypertrophied beyond the needs of the circulation,"³ so that it gets prematurely beyond the feeding power of its arteries, and the final and irremediable breakdown of compensation thus inaugurated and hastened by the very means employed to avert it.

It is a curious commentary on the changes in medical opinion that in these latter days the production of active hypertrophy of the heart should be ascribed to that drug, which, for the first half of this century, was thought to be a

² Bälz, *Archiv der Heilkunde*, 1876, S. 468.

³ *Edinburgh Medical Journal*, April, 1895, p. 871.

sovereign cure for that affection. Neither opinion is founded on either pathology or fact. We have many drugs which produce atrophy. I know of none that cause hypertrophy. Hypertrophy of a muscular organ is the result of a call for increased exertion, and arises in no other way. The heart has a large reserve of energy, and even when called upon for increased exertion does not at once hypertrophy; it is only when dilatation has occurred that the needful compensating hypertrophy follows. And so throughout the future progress of the affection the dilatation is ever in advance, the hypertrophy lags somewhat behind. Digitalis increases the elasticity and improves the nutrition of the myocardium, and enables it to withstand the dilating influences to which it is subjected. Far from unduly stimulating the heart and forcing upon it a needless hypertrophy, the tonic action of digitalis checks the progress of dilatation, and retards instead of precipitating hypertrophy.

Corrigan long ago raised a warning voice against the use of digitalis in aortic regurgitation, because he looked upon it as a pure sedative, and regarded the prolongation of the diastole as a source of increased danger to the heart. It is an indication how ill understood the true action of digitalis still is that a similar idea is yet held by some. But the increased elasticity and energy that the myocardium acquires from the action of digitalis is not only sufficient to enable it successfully to resist the dilating influences to which it is exposed during the prolonged diastole, but is even adequate to produce a certain amount of contraction of the ventricular cavity, as shown by the recession of the apex beat upwards and to the right.

About a couple of months ago I found an old professional friend suffering from the effects of influenza upon a heart labouring under aortic regurgitation. I prescribed digitalis for him, and a fortnight afterwards asked him to detail his experience for your benefit. In his case the regurgitation is simple, and without mitral complication.

He writes: "When first I saw you my pulse was irregular and feeble. In the morning I could only walk about 250 yards. This took me from nine to twelve minutes, and I had to pause to gain breath three or four times on each occasion. In the afternoon, with usually the assistance of an arm, I could walk half a mile, resting say three times, but being troubled with occasional dull pain in the heart, constant distress from a feeling of constriction in the lungs, and a feeling of strain and weakness in the muscles. My stride was little more than half its natural length; and this half mile took me always over half an hour to accomplish. The night before I first took the digitalis was the most trying and distressing which I can remember. My breathing was just a succession of rapid gasps, which ceased whenever I seemed about to fall asleep, when I had to draw a breath by an effort of will. The inhaled air did not seem to get fully into the chest. There was mental confusion, if not absolute cowardice. The feebleness and irregularity of the pulse were extreme, and my condition was altogether so painful that a sense of duty alone restrained me from desiring death. I had to walk all night till 5 in the morning. After the first day of taking digitalis all this was for the most part changed. Even then, as I expressed myself to you, I was 'a different man.' I think anyone might be satisfied who has a pulse like mine now, I sleep well, the stride has lengthened out, five to six minutes now suffice for the 250 yards; with sometimes no rest at all I have walked about a mile and a-half. Though there is occasionally a little panting, the air seems to get to the bottom of my chest, which is altogether free from any feeling of constriction. In fact, for a week I have been enjoying life, there is a kick in my pulse which tells of everything firming up, and there is not in my mind an atom of doubt as to the *post hoc propter hoc* in my case.—Ever yours, M. F. H."

Much as digitalis can do, it acts within certain limitations, and it fails occasionally when we most desire its success. It has no action whatever on the often protracted ingravescent asthyle of a moribund heart, but as we are not always able at once to recognise this form of terminal failure we are bound to employ that remedy which holds out most hope, but we have no right to be disappointed when it fails. Since the days of Withering it has been known that when "the limbs in anasarca are solid and resisting we have but little to

hope" from digitalis. But in these cases as soon as the tension is relieved by purgation, or local drainage from incisions, digitalis acts well, the rest of the fluid is absorbed and the heart improves. In dilatation of the right ventricle following marked stenosis of the mitral valve, or originating in that limitation of the area of the pulmonary capillaries always present in emphysema of the lungs, we cannot expect much from digitalis, it acts as a tonic and improves the condition of the heart, but it cannot in either case contract the right ventricle because of the permanent and incurable nature of the obstacle to the circulation that has produced its dilatation. Where loss of arterial elasticity from any cause has produced dilatation of the left ventricle digitalis acts badly, and may even increase the dilatation unless it is combined with some vascular stimulant, but with this proviso it acts well and is most useful in all such cases. Lastly, digitalis is said to act badly or to be even positively injurious in cases of fatty heart. But as hearts diagnosed as fatty are as a rule only feeble and dilated it would be a sad mistake to be deterred from giving such hearts all the benefits they are so likely to receive from digitalis by the baseless dread of an unrecognisable chimera. I may add that I have never seen any damage accrue from acting on this principle.

The most suitable preparations of digitalis to employ are first of all the powdered leaves carefully prepared, and not over a year old. The infusion ranks next to the powdered leaves; it seems to contain all the most active principles of the plant, and it lends itself readily to combination with vascular stimulants, which are so often necessary adjuncts to secure the full benefit of the remedy without discomfort to the patient. From the very small dose of the powdered leaves employed it is scarcely necessary to have recourse to any more concentrated preparation, but Nativelle's and Merck's digitalin are both active and convenient preparations, and are useful when merely a cardiac tonic is required; if given in larger doses for any other purpose they are both prone to excite nausea, and do not act so favourably as either the leaves or their infusion. The tincture is an intermediate preparation; it acts well as a tonic, and combines readily with other tonics, less readily with vascular stimulants; it ranks next to the infusion, and is a suitable and convenient form in which to employ the remedy.

To enter more at large into the various combinations of remedies or of other forms of treatment that may be advantageously conjoined with digitalis in the treatment of different heart affections would plunge us into the wide field of general cardiac therapeutics, into which I have no intention to enter at present.

In conclusion I have only to add that with attention to the selection of a suitable dose, and the ordinary precautions which every form of treatment demands, if we are to expect any benefit from it, digitalis will do everything that can be reasonably expected of it, and will confer more benefit on cases of cardiac disease than any other drug in the *Pharmacopœia*; not because it is a diuretic, a sedative, or a stimulant to the heart, but because it maintains and improves its metabolism: for failure of metabolism is, under all circumstances, the great source of danger to that important organ.

Professor LÆSCH said that the influence of digitalis as a tonic and sedative was a question of dosage. Such doses as Dr. Balfour had indicated were free from danger; yet in some cases very slightly larger doses may easily affect the heart and do unforeseen harm. The readiness with which comparatively small doses render the heart's beat unduly slow or irregular points to real danger from slight excess of dose, and although it is impossible to judge when a patient dies with heart disease taking digitalis, there have not been wanting cases in which it was indicated that the digitalis was to blame. It is worthy of notice that in experiments on the excised heart of the frog the cessation of the heart's action is usually permanent; there is no such recovery when the poison ceases to circulate through the heart, as we see in the case of some other drugs. This points in the direction of the view that in cardiac diseases digitalis may readily become a dangerous remedy. The records of the treatment in pneumonia show that in this ailment digitalis can usually be given without danger, and the same seems to be the case in delirium tremens.

Dr. ILLINGWORTH did not consider that digitalis was a cardiac tonic. If given in doses of 6 to 10 minims in cases of pneumonia, the pulse-rate might be very considerably reduced, and syncope or even death might occur. He considered this to indicate a depressant or calnative action. He admitted, however, that in cases of nervous palpitation the pulse-rate appeared to be slowed and the volume increased, but in his opinion this was a mere side issue, and not a main question.

THE SUBCUTANEOUS USE OF CREASOTE AND GUAIACOL IN PULMONARY PHTHISIS.¹

By F. R. WALTERS, M.D., M.R.C.P.,

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Of all the drugs which have been used in the treatment of phthisis there are probably none which have been so widely adopted as wood creasote and its derivations. Advocated in 1833 by Reichenbach, condemned in 1835 by Martin Solon, it fell into disrepute until revived by Bouchard and Gimbert in 1877, since which it has been tried and approved by a long list of authorities—Jaccoud and Dujardin-Beaumetz, Dieulafoy and Germain Sée, Sommerbrodt, Von Brun and Guttman, Douglas Powell, Burney Yeo, and many more, who all agree as to its utility, while they differ as to its mode of action, dosage, and modes of administration. At the present time some are enthusiastic in its praises while others are as strongly opposed to it; and it must be admitted that it has a nasty way of failing in some of the cases where its help is most needed. It is, however, not surprising that this should be the case. To begin with, in a disease like pulmonary phthisis, where destruction and repair go on side by side, and the same process is sometimes useful and necessary, at other times disastrous, it is very difficult to estimate the effect of any remedy, owing to the impossibility of obtaining strictly comparable cases. In the next place, not only is there true or wood creasote and sham or coal-tar creasote, but several varieties of wood creasote, such as pinewood creasote, which contains more cresols, and beechwood creasote, consisting largely of guaiacol; and even beechwood creasote (which is usually preferred) varies in its composition. To add to these difficulties, the dose of creasote which can be borne with impunity varies considerably with individual idiosyncrasies and with the type of the disease, perhaps more than is the case with any other commonly used drug. Bearing these facts in mind, it is not so much remarkable that authorities should differ as to its utility as that there should be as great a unanimity. The concord becomes more striking than the discord. The number of cases dealt with by some of these observers is so considerable that there is at least strong *prima facie* evidence, in favour of the utility of the creasote compounds.

Bouchard in his first paper gave the results of 93 cases, and subsequently published more; Sommerbrodt's cases numbered over 5,000, Von Brun's 1,700.

Bouchard and Gimbert's early results were obtained by the administration of comparatively small doses of creasote—3 to 6 minims—over long periods of time, although they subsequently increased their doses in certain cases. They gave it either in cod-liver oil, or in alcohol with a bitter tonic on an empty stomach. Sommerbrodt, writing in 1887, recommended the administration of three capsules, each containing 1 minim of pure beech-wood creasote, increasing the dose by one daily until the eighteenth day, when this quantity (20 minims) was to be continued for many months.

As a rule patients can be readily brought in one way or another to tolerate large doses if these are sufficiently gradually increased; but it is by no means certain whether more than 15 or 20 minims per day can be absorbed by the alimentary canal, judging by Poggi's results with guaiacol. And some patients are quickly nauseated by quite small doses which do not appear to be of any use. To overcome this difficulty several methods have been adopted. A less irritating ingredient may be given, such as guaiacol, introduced by Sahli in 1887, or the creasote may be prescribed

with some bland fluid such as milk, or with a gastric sedative. Another method is to give it in capsules, or in keratin-coated pills which are only dissolved beyond the stomach. The administration of carbonate of guaiacol or creasote depends on a similar principle, as the combination is only exceptionally broken up in the stomach.

There seems to be some doubt as to the equal efficacy of guaiacol and creasote, the experiments of Main² appearing to show that the crude drug was more reliable. Hudeod, of Geneva, is strongly impressed with the advantages of rectal administration, and Burlureaux also adopts this method amongst others. Germain-Sée has recently advocated the employment of inhalations of compressed air containing creasote. Another plan is that of external applications, as guaiacol has been shown to be largely absorbed by the skin. But the method which I wish to dwell upon to-day is that by subcutaneous injection. This has been adopted in one form or another by Schetelig, Picot, Diamantberger and Weil, Burlureaux, and others. Schetelig uses 20 to 30 per cent. solutions of creasote in oil of cloves, injecting 16 minims into the thigh or abdomen from four to twelve times daily, leaving the needle in and applying gentle massage between the injections, which are repeated at intervals of a quarter of an hour to an hour. He states that, although the taste of creasote was sometimes noticed after the injection, there was no digestive disturbance, and marked antipyretic effects were observed. He gives guaiacol in the same way, in one-third to one-fourth the dose. Meunier, of Lyons, prefers liquid vaseline as a medium. Picot, of Bordeaux, injects a mixture of sterilised olive oil and vaseline containing 1 per cent. iodoform and 5 per cent. guaiacol, beginning with 1 c.cm. of the mixture and increasing to 3 c.cm. He remarks that no swelling or other local reaction follows. Burney Yeo has used the same method with a more concentrated formula.

The method, advocated by Diamantberger and Weil at the Paris Congress for Tuberculosis in 1891, was to inject creasote dissolved in an equal volume of sterilised almond oil. Of this they injected two Pravaz syringefuls in twenty-four hours, and after over 1,000 injections have had no accidents. Shingleton Smith adopts this method. Prévost, on the other hand, declares that a chemical combination of guaiacol with oleic acid is much less irritating than a mere oily solution. The chief advocate of the subcutaneous injection of oily solutions of creasote and guaiacol is Burlureaux, of the Val de Grâce. He lays stress on the importance of using a pure preparation such as creasote prepared by Choay's method dissolved in sterilised olive oil free from oleic acid, and on the gradual introduction of large quantities into the body up to the capacity of the individual, which is a variable quantity. He uses a special apparatus originally contrived by Gimbert and modified by Guerder and himself, one form of which I am able to show you to-day. The oily solution is driven into the body by atmospheric pressure, the degree of which is indicated by a manometer. Not more than 20 grammes (say 5 fluid drachms) per hour must be introduced, so that as most of his patients receive from 50 to 100 grammes of creasoted oil per diem at the height of the treatment, a single injection may last several hours. He begins with 5 grammes of a 1 in 15 solution, and if there are no signs of intolerance increases it to 50 grammes or more. One of his patients received 5 kilos. under the skin in as many months, besides 1 kilo. per rectum. This represents between 30 and 40 minims of pure creasote per day. The largest quantity which appears to have been injected at one sitting was 220 grammes, or nearly 8 ounces, of a 1 in 15 solution. Some patients of his were, however, less tolerant, as in one case 5 grammes of a 1 per cent. solution caused distress. Whenever small doses are persistently badly borne, he regards the prognosis as highly unfavourable. Where the treatment is doing good the appetite improves, flesh is gained, and the local lesions show signs of healing. Intolerance is shown by shivering, perspirations, and a condition resembling the collapse of pernicious malarial fevers, with or without high temperature. A persistent taste of creasote or black urine are of bad import when they come after small doses.

To come to my own results, which are unfortunately incomplete, as some of my notes have been mislaid or not yet returned. I have had some 6 or 8 cases treated in this

¹ Read in the Section of Pharmacology and Therapeutics at the Annual Meeting of the British Medical Association held in London, July-August, 1895.

² Bull. de Thérapie, cxxii, 205.