ON THE TREATMENT OF ANÆMIA AND CHLOROSIS BY THE CHIEF IRON PREPARATIONS COMMONLY IN USE.

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(Concluded from page 355.)

CASE 10. — M. M., aged twenty-two, was admitted to Ward 30 on July 19th, 1892, with symptomatic anæmia, the red corpuscles being about 2,000,000 per c.mm. and the hæmoglobin 20 per cent. The patient was on admission, prescribed sulphate of iron, seven grains thrice daily. In fourteen days the corpuscles had increased to 3,200,000 per

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c.mm. and the hæmoglobin to 40 per cent., and at the end of thirty-five days' treatment the patient was discharged cured, the corpuscles being 5,700,000 per c.mm. and the hæmoglobin 62 per cent.

Treatment.—Sulphate of iron: This case well shows the superior efficacy of this iron salt in its comparatively quick and reliable effects in all anæmias and in chlorosis, and in the uniformity of its beneficial effects alike upon the blood cells and hæmoglobin.

Progress.

Date.	Red corpuscles.	Hæmoglobin.
July 17th ...	1,900,000 per c.mm.	32 per cent.
Aug. 4th ...	3,200,000 "	40 "
" 11th ...	4,000,000 "	48 "
" 18th ...	4,300,000 "	60 "
" 24th ...	5,700,000 "	62 "

CASES 11 AND 11A.—J. C. and A. C. were admitted to Ward 33, the one on Nov. 11th and the other on Nov. 28th, both suffering from symptomatic anæmia and nearly in the same degree, except that it was somewhat more advanced in the former and consequently somewhat longer delayed in recovery. Both patients were put upon the same remedy—viz., the saccharine carbonate of iron, twenty grains being given to each, thrice daily, with meals. Between Nov. 11th and Dec. 13th the red corpuscles had increased from

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3,400,000 per c.mm. to 6,000,000 per c.mm. in J. C.'s case, and the hæmoglobin from 52 per cent. to 68 per cent., at which time the patient left the hospital cured, the duration of treatment being thirty-two days. The red corpuscles in A. C.'s case at the date of admission (Nov. 28th) were 3,800,000 per c.mm. and the hæmoglobin 55 per cent., and on Dec. 17th,

when she left the hospital cured, they had increased to 5,500,000 per c.mm. and the hæmoglobin to 76 per cent.

Treatment.—These cases of treatment by the carbonate of iron may be taken as fairly showing the effects of this preparation of iron in cases of symptomatic anæmia and chlorosis. As a remedy it is well borne in all cases, and is rapid and curative in its effects. It is on these accounts entitled to rank as among the best of our iron remedies, and second only to the sulphate of iron, if not, indeed, upon a par with it.

CASE 12.—J. S., aged twenty, was admitted to Ward 33 on Oct. 24th, 1892, with well-marked symptomatic anæmia and a progressive history of the disease. The red corpuscles were 3,400,000 per c.mm. and the hæmoglobin 52 per cent. The

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diet being carefully arranged to suit her impaired digestion, she was put upon the protochloride of iron, one drachm thrice daily after meals.

Treatment.—This treatment was continued for sixty-five days, with the result that at the end of that time the red blood cells had increased to 6,500,000 per c.mm. and the hæmoglobin stood at 79 per cent. The drawback to the remedy was its causing sickness with vomiting, on account of which it had to be more than once suspended for a few days at a time, whereby the duration of the treatment was protracted. To avoid this it should be given in smaller doses to begin with, until toleration of the remedy is induced, increasing it from half a drachm to one drachm. Making allowance for this drawback in the use of the protochloride and the consequent delay in effecting cure, it should be ranked as one of the most efficient remedies.

Progress.

Date.	Red corpuscles.	Hæmoglobin.
Oct. 25th ...	3,000,000 per c.mm.	52 per cent.
Nov. 6th ...	3,200,000 "	55 "
" 13th ...	3,500,000 "	58 "
" 20th ...	3,700,000 "	62 "
Dec. 9th ...	5,500,000 "	76 "
" 16th ...	6,200,000 "	78 "
" 29th ...	6,500,000 "	79 "

CASE 13.—M. W., aged eighteen, was admitted to Ward 33 on Nov. 5th, 1892, suffering from advanced chlorosis. Her condition was characterised by unusual pallor, prostration, palpitation, with loud hæmic murmurs in the neck and at the base and apex of the heart, amenorrhœa, and a severe type of atonic dyspepsia—the gastric contents showing absence, in a marked degree, of free hydrochloric acid. An examination of the blood showed 3,000,000 per c.mm. of red blood corpuscles, with only 32 per cent. of hæmoglobin. The patient's condition presented a suitable opportunity of testing how far her anæmic state had been brought about in consequence of the atonic dyspepsia which had preceded and accompanied it—more especially with reference to the absence of free hydrochloric acid—so marked a feature in her dyspepsia. I accordingly decided to treat her with hydrochloric acid in the first instance. The treatment was begun on the sixth day after her admission, 100 minims of the dilute acid being given daily in 25 minim doses at a time. Between Nov. 11th and 13th—that is, seven days after the commencement of treatment—the enumeration of red corpuscles and percentage of hæmoglobin remained stationary, the patient, however, taking food much better and her dyspepsia being entirely relieved. From that date to Dec. 16th the red corpuscles increased to 4,000,000 from 2,000,000 per c.mm., but the hæmoglobin remained at 35 per cent., the latter having only increased by 4 per cent. during a period of thirty-six days. This increase was no doubt

owing to the action of the phosphate of iron which was given during the last week of this period in 24-grain doses daily. At this stage of imperfect recovery the patient left the hospital to go to her home in the country, much against my wish ; so that we lost from that time all further account of the case. I have no doubt, however, that had she remained

recovery from anæmia, very probably by its improving some constitutional defect upon which the anæmia may partly depend.

CASE 15.—Mrs. A——, aged fifty-three, came under my observation in the autumn of 1891. An examination showed the red corpuscles to be reduced to 600,000 per c.mm. and the hæmoglobin to 10 per cent. The irregular shapes which characterised the blood discs, the splenic enlargement, the lemon tint of the patient's complexion and her general cachexy left me in no doubt that the disease was pernicious anæmia, and I cite her case to show, by contrast, that while exhibiting iron and other tonics of the same class there was no evident improvement in the amount of hæmoglobin or in the number and character of the red cells until arsenic was added to the treatment. Fowler's solution of arsenic was commenced in five-minim doses thrice daily, which was gradually increased to over double that quantity. This treatment, combined with full doses (ten grains three times a day) of the citrate of iron and quinine, with a specially good dietary, enhanced by the addition of port wine and maltine, after many weeks brought about an improvement in her condition, well shown by the red corpuscles having increased to 2,480,000 per c.mm. and the hæmoglobin to 50 per cent. At this

under the hydrochloric acid treatment the red corpuscles would have been restored to their normal number. But it is evident, from the low standard at which the hæmoglobin remained, that her condition would eventually have resulted in her disease being uncured, seeing that the defect of hæmoglobin constituted the essential feature of her anæmia, which, as I have already pointed out in previous cases, is the pathological feature which distinguishes chlorosis from symptomatic anæmia on the one hand and from pernicious anæmia on the other. It follows from the results of this trial that while hydrochloric acid is of great value in improving the tone of the digestive functions generally, no doubt by favouring the digestion of the proteids, it nevertheless fails by itself to restore the hæmoglobin ; so that in chlorosis, as in symptomatic anæmia, and even more so, it is necessary to have recourse to some form of iron in order to establish perfect recovery.

CASE 14.—A. H——, aged twenty-six, was admitted to Ward 30 on Nov. 3rd, 1891, with symptomatic anæmia and secondary erythema nodosum. The red corpuscles were reduced to 1,590,000 per c.mm. and the hæmoglobin to 35 per cent. The patient was prescribed 5 minims, increased to 10, of arsenic (Fowler's solution) thrice daily. After fifteen days the patient expressed a wish to leave the hospital to return to her employment. By that time the corpuscles had increased to 3,850,000 per c.mm. and the hæmoglobin to 59 per cent. The

stage in the course of her treatment, at her own request, she left the hospital for her home in the south of Scotland, where she is at present, much in the same condition of health as at the time of her discharge. It should be added that she was under arsenical treatment while in hospital for a period of three months.

CASE 15.

Corpuscles balloon-shaped, tailed, crenated with a number of microcytes.

Progress.

Date.	Red corpuscles.	Hæmoglobin.
Aug. 25th	640,000 per c.mm. ...	10 per cent.
Sept. 3rd	910,000 ,, ...	15 ,,
„ 14th	1,450,000 ,, ...	35 ,,
„ 30th	1,810,000 ,, ...	50 ,,
Nov. 4th	2,480,000 ,, ...	45 ,,
Dec. 1st	2,160,000 ,, ...	35 ,,

GENERAL CONCLUSIONS.

1. *Sulphate of iron.*—Of the varieties of iron used in the trials here recorded, the best results have been obtained from the sulphate. This accords with previous experience. It is the preparation which undoubtedly possesses the greatest therapeutical activity, and the one which in the different varieties of the disease and constitutional differences of the anæmic patients may most uniformly be depended upon for satisfactory results. In anæmic patients who suffer markedly, as many of them do, from atonic dyspepsia, and in whom consequently the hydrochloric acid is either greatly deficient or absent, it is of great advantage to their recovery to prescribe from fifteen to twenty-five minims of dilute hydrochloric acid shortly before meals, the iron salt being taken shortly after meals. But on the contrary, to those patients whose stomach complaints are of an opposite nature, being due to excess of acid (pyrosis), acid in any form cannot be given ; the substitution of ten grains each of bicarbonate of soda and carbonate of potash before meals will be of material assistance to the stomach by inducing tolerance of the iron and thereby ex-

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arsenic in this case must be regarded as only indirectly promoting the restoration of the blood cells and hæmoglobin by its direct and primary effect upon the constitutional condition with which the erythema was connected, the anæmia being only a secondary sequence to it. We have, however, had many proofs that arsenic when given combined with the irons coöperates beneficially in some cases in expediting

pediting recovery. In assigning the first place to the iron sulphate as a remedy, I am guided by the whole of the circumstances connected with each of the cases in which the trials were made. As a remedy, it is exceptionally active in restoring the deficient corpuscles, alike in their number and character, and is also notably active in restoring the hæmoglobin in chlorosis.

2. *Carbonate of iron (saccharine)*.—Numerous trials with this preparation, only two results of which are shown on the charts (see Cases 11 and 11A), were uniformly of a favourable character in the different types and stages of the disease in which it was given. It is invariably well tolerated, whatever be the nature of the dyspepsia from which the patient suffers. It was given in doses varying from twenty to thirty grains thrice daily during or immediately after meals. On these grounds I consider it entitled to rank as the second best therapeutic iron.

3. *Protochloride of iron*.—This preparation was prescribed in the form of the syrup in one drachm doses thrice daily after meals. Each drachm of the syrup contained seven grains of the protochloride. As, during its administration, it repeatedly brought on nausea and had consequently to be suspended for a time, it would be better to avoid this drawback by giving it at the commencement in smaller doses, increasing it gradually to the one drachm dose as mentioned above. Making allowance for the delay caused in this way by the suspension of the remedy and its liability to induce intolerance, it is entitled to at least hold a third place in the grade of efficacy of these remedies. Recovery under its administration is otherwise in every respect satisfactory and complete.

4. *Phosphate of iron* yielded excellent results only in some of the patients treated by it, but in others it apparently failed, its effects being only appreciable after considerably protracted treatment. The beneficial character was apparent in those types of the disease in which there existed constitutional conditions allied to neuroses.

5. *Iron protoxide*.—This iron in some cases yielded only negative results, but in other cases its effects were satisfactory. This difference in its effects may depend upon individual peculiarities of constitution. It cannot therefore as a remedy be relied upon in all cases.

6. *Arsenic*.—This remedy when combined with iron is evidently useful as an alterative; but, as the result of the trials made with it as the sole remedy showed, it did not appear to exert any direct or appreciable effect on the renewal of the red blood-corpuscles and hæmoglobin in the cases of symptomatic anæmia and chlorosis in which it was tried. When, however, combined with an iron, especially the sulphate, I could not avoid being convinced that the efficacy of the iron was enhanced by the combination.

7. In pernicious anæmia, however, as is well seen in Case 15 (see chart), arsenic exerts a distinctly noticeable effect in promoting recovery alike of red blood-corpuscles and hæmoglobin. Although iron was long and freely exhibited in Mrs. A.—'s case, no evident effects of a constructive kind were produced upon the corpuscles and hæmoglobin until arsenic was added to the treatment; and not even then until full doses (20 to 30 minims daily) had been continued for some time. It is, however, rare, and indeed exceptional, in pernicious anæmia, to be able to administer arsenic in almost any dose, except the smallest—that is only a few minims daily—on account of extreme intolerance of it, so that in the majority of cases it is practically out of account as a remedy.

8. It will doubtless have been observed that, in several of the cases referred to, the red corpuscles numerically exceeded, in some instances by 2,000,000 per c.mm., the usual standard number of 5,000,000. This excess having been found repeatedly, I am led to believe that by the treatment being continued a similar result would have been obtained in most, if not in all, the cases. It would appear from this discrepancy that an estimation of red corpuscles at 5,000,000 per c.mm. is too low a standard.

9. On the other hand, speaking with reference to the hæmoglobin, I must observe that I have never yet succeeded in raising the hæmoglobin to a standard of 100 per cent. The highest obtained has never exceeded 90 per cent., and that amount only in instances of exceptionally robust health. My experience therefore leads me to believe that 80 per cent. is a good health standard; and that 70 per cent., or even under, may be taken as a fair average estimate at which patients may be discharged from hospital treatment, provided that the red cells are over 4,000,000 per c.mm. It would appear from these results that our views in regard to the relative

estimation of the red corpuscles and hæmoglobin require to be modified in accordance with these trials.

10. I have repeatedly had occasion to notice certain differences between symptomatic anæmia and chlorosis which I have not before seen referred to, but which are of importance as diagnostic signs. In the former the red cells and hæmoglobin do not bear the same definite relation to one another in their decrease and increase which may be observed in symptomatic anæmia. I have several times recorded cases of advanced chlorosis in which there was present a high numerical standard of red corpuscles (over 5,000,000 per c.mm.), while at the same time the hæmoglobin did not exceed 25 per cent. Such cases might not improperly be designated hæmoglobin anæmia, in the same sense that we speak of a pernicious anæmia as corpuscular. The low standard of hæmoglobin in chlorosis represents the chief pathological feature in that disease as do the reduced numbers and defective morphological characters of the red globules in pernicious anæmia. In consequence of the comparatively slow recuperation of the hæmoglobin in chlorosis the recovery of these cases is longer delayed than in those of symptomatic anæmia, and, besides this, there is observed in the red globules a decided proclivity to undergo morphological degenerations. These special differences lead us to regard chlorosis pathologically as a graver type of anæmia than symptomatic anæmia, although at the same time it specifically differs from the pernicious kind.

11. I would here again revert to the very severe type of anæmia referred to at the outset as being put under treatment by hydrochloric acid as the sole therapeutical remedy. I am not aware of this treatment having previously been tried. Many anæmias doubtless originate in defects of the primary gastric digestion caused by either deficiency or complete absence of free hydrochloric acid in the stomach, the consequence of which is that the proteids not undergoing normal metamorphosis are largely thrown out of the system as waste and lost. This method of treatment by hydrochloric acid can only be of use in cases in which there is present that condition of atonic dyspepsia in which the hydrochloric acid is, as I have said, markedly deficient or entirely absent. This type of dyspepsia, however, is characteristic of a large number of anæmias at the commencement of, as well as throughout, their entire course. The result of the trial by hydrochloric acid will be seen by referring to Case and Chart 13. During the forty-two days the patient was under this treatment the red corpuscles increased from 2,500,000 per c.mm. to 4,200,000 per c.mm., and during that long period the hæmoglobin only rose from 30 per cent. to 36 per cent. The patient at this stage of incomplete treatment left the hospital of her own accord. It was evident, however, that, whilst longer continued treatment would have raised the corpuscles to 5,000,000 per c.mm., it would not have materially increased the hæmoglobin from the low standard at which it had apparently become stationary. The result of this clinical experiment, as that of every other, proves that iron in some form is absolutely indispensable in the treatment of chlorosis, as well as of symptomatic anæmia, to effect complete recovery.

12. In each of the anæmias here reported there co-existed chronic constipation, and the urine in each case yielded the roseate colour, with nitric acid, referred to by M'Munn in his "Chemistry of the Urine," as an indication of the destruction of red blood cells. To what extent, if at all, this colour reaction indicates blood destruction through the agency of reabsorbed toxic materials from the prima via, as Sir Andrew Clark suggested, remains to be determined by further investigation.

The following anatomical and pathological distinctions have been suggested in the course of these trials as marking off diagnostic differences between the three grades of anæmia: (1) In symptomatic anæmia there exists a constant proportional relation between the number of red corpuscles and the amount of hæmoglobin. They diminish relatively during the course of the disease and increase relatively during recovery, the iron being deficient as to the whole blood and each cell relatively. (2) In chlorosis the relation between the number of red corpuscles and the hæmoglobin is entirely broken. The hæmoglobin is markedly deficient relatively to each cell and to the whole blood. The low relative amount of hæmoglobin is the chief pathological determining feature in chlorosis and points to the low amount of iron, which in this type of the disease is *par excellence* to be regarded as the specific remedy in its treatment. (3) In pernicious anæmia the normal relation between the red cells and the hæmoglobin is also disturbed. The iron is in excess in each

cell and also in proportion to the whole blood. The great diminution in the number of the red corpuscles and the relative excess of the hæmoglobin in relation to these and to the whole blood are the distinguishing features in this anæmia, so that, as chlorosis may be regarded as a hæmoglobin anæmia, pernicious anæmia may be viewed as a red corpuscular anæmia, that being the chief point of distinction between them. The excess of iron present in the blood of pernicious anæmia plainly contra-indicates its employment in the treatment of that disease, except in small quantities, as an alterative. Arsenic (Fowler's solution) when tolerated and continued by a patient suffering under pernicious anæmia is the preferable remedy. It is, however, only borne in certain cases, and in every case the toleration of it is to be acquired by giving it in small doses at the beginning and gradually increasing it. Quinine is markedly useful in that group of pernicious anæmias in which there is splenic enlargement, and its beneficial effects are enhanced when combined with moderate doses of iron. The best drug in such a case is the citrate of iron and quinine given in full doses. My recent experiences in connexion with the treatment of pernicious anæmia by the transfusion of healthy blood is leading me to attach much importance to that mode of treatment.

A CASE OF LACTIC FERMENTATION IN THE BLADDER.

WITH SUGGESTIONS FOR THE USE OF THE LACTIC FERMENTATION AS A COUNTER-SEPTIC AGENT IN CASES OF AMMONIACAL DECOMPOSITION OF THE URINE AND IN THE TREATMENT OF PUTREFACTIVE WOUNDS AND SORES.

By SIR WILLIAM ROBERTS, M.D., F.R.S.

SOME months ago I was consulted by a man eighty-four years of age. He looked unusually young for his years and was in excellent general health. He informed me that he had undergone the operation of lithotripsy five years before. The procedure was carried out without difficulty, and the bladder was soon declared to be free from calculous fragments. He was, however, advised to use the catheter, as he was unable to completely empty the bladder. He has used the catheter ever since: at first twice a day, and for the last two years once a day. He is now able to void the urine in the natural way, but he is not able to empty the bladder completely except with the aid of the catheter. There is very little irritation of the urinary passages, and he is not usually disturbed to relieve the bladder more than once during the night. He brought with him a freshly voided sample of his urine. The specimen was a remarkable one, and strongly arrested my attention. It was very turbid, intensely acid and contained sugar. Examined under the microscope it was found loaded with bacteria, in the form of micrococci and bacilli, resembling those which are seen in souring milk. There were also numerous torulæ, having the characteristic appearance of yeast cells. Besides these adventitious organisms there existed a good many pus corpuscles and a corresponding (small) amount of albumen. I had several subsequent opportunities of examining the urine; on one occasion the sample was withdrawn by catheter in my room and examined in the absolutely fresh state. All the specimens presented the same essential peculiarities. They were all sharply acid and saccharine and contained myriads of bacteria and numerous yeast cells. The patient complained of none of the usual symptoms of diabetes (there was neither thirst nor diuresis); but he reported that some time ago, for a period of three weeks, he suffered from urgent thirst and an excessive flow of urine and that sugar was then found in the urine by his medical attendant. A remarkable feature of the case, from a clinical point of view, was the maintenance of a sharply acid reaction of the urine and the absence of recurrent formation of phosphatic concretions in the bladder. Here was an old man who had undergone the operation of lithotripsy five years ago, who was unable to completely empty his bladder, who used the catheter daily, and who, nevertheless, remained free from ammoniacal decomposition of the urine and free from phosphatic

concretions. Conditions more favourable for the supervention of these events could scarcely be imagined—why did they not occur? The explanation, I think, is as follows. The patient is glycosuric; he was probably glycosuric at or near the time of the operation and has continued so ever since. The air and water around us are full of micro-organisms of diverse kinds which are capable of exercising a fermentative action on organic compounds. One group (the lactic ferment, the alcoholic ferment, and the acetic ferment) tend to produce acids; another group (the ammoniacal ferment of the urine and the ferments of common putrefaction) tend to produce carbonate of ammonia. When the germs of these various ferments fall simultaneously and promiscuously into an organic fluid such as the urine there is a conflict for supremacy, and it depends on the composition of the fluid which group shall obtain the mastery. In a non-saccharine urine the issue of the conflict is always in favour of the ammoniacal fermentation, but if the urine be saccharine the issue is always in favour of the acid fermentation. This point was proved experimentally in the laboratory.

In the bladder of this patient three fermentations tending to acidity appeared to be going on concurrently. The chief of these was the lactic fermentation, and lactic acid was identified as the main cause of the intense acidity of the urine. The second was the alcoholic fermentation engendered by the yeast cells, which were always present in the patient's urine. The third was the acetic fermentation, for acetic acid was clearly demonstrated in the distillate from the urine. I failed to obtain direct proof of the presence of alcohol in the urine. The alcoholic fermentation was probably only feeble in degree, and presumably the alcohol generated was usually changed, as fast as produced, by the agency of the acetic ferment into acetic acid. The patient, however, remarked that the urine sometimes had a "vinous smell," so that probably the urine did sometimes contain alcohol. There is no difficulty in accounting for the introduction of the germs of these ferments into the bladder in the present case. The catheter which was daily used furnished a well-recognised means of conveyance, and the patient admitted that he was not over-careful in the observance of antiseptic precautions. Finally, it may be confidently predicted that if the patient at some future time ceased to be glycosuric and still went on using the catheter in his careless way the urine would in no long time be in the grip of the ammoniacal fermentation, and he would then stand in danger of the formation of phosphatic concretions in the bladder. His glycosuria, in fact, protects him from this untoward contingency.

This case gives rise to the suggestion that the lactic fermentation might be turned to therapeutic uses. This agent might be tried in intractable cystitis from ammoniacal decomposition of the urine and in recurrent phosphatic formations after operations for stone. The mischief in these cases is contingent on the establishment of the ammoniacal fermentation in the bladder, whereby urea is changed into carbonate of ammonia. This change, if it goes far, renders the urine irritating to the mucous membrane and provokes cystitis; it also imparts an alkaline reaction to the urine, with consequent precipitation of the mixed phosphates. Now, if we could start and maintain in the bladder a counter-fermentation of the lactic type (and this depends on the presence of sugar), the irritating quality of the urine would be diminished, its acidity would be restored, and the further deposition of phosphates would be prevented. Attempts in this direction might be made by injecting into the bladder a saccharine solution which was in process of lactic fermentation. In casting about for a practical method of carrying out this idea the first suggestion was sour milk, or, rather, sour whey. Souring milk is the typical lactic fermentation. It was, however, found to be somewhat difficult to prepare sour whey in a fit state for injection into the bladder. After sundry trials in various directions the conclusion was reached that for the purpose in hand malt extracts were probably the best available source of a suitable lactic fermentation. The extract of malt termed "bynin" is, from its liquid character and easy miscibility with water, especially convenient for the suggested purpose. Bynin (like other extracts of malt) is already impregnated abundantly with the germs of the lactic ferment, and when it is diluted with ordinary water it passes at once spontaneously into lactic fermentation. Experiments made in the laboratory indicate that water containing from 10 to 20 per cent. of bynin would make a suitable solution. An ounce or so of such a solution might be injected once, twice or thrice a day into the emptied