

sordes round the lips. The temperature varied from 100·5° to 102° and the pulse was very rapid, reaching 150 or even 160. There were no signs of uterine or pelvic mischief. She was unable to answer questions. On the 14th she had a very quiet night, the movements being very slight. On the 15th the patient was very restless and was ordered 30 grains of chloralamide every four hours. She slept for eight hours on the night of the 16th. She had a morbilliform rash over the face, the arms, and the chest. The choreic movements were marked but were certainly better. On the 19th the patient was very much better, the temperature being normal and the pulse 102. The rash was gone and the uterine condition was normal. On the 22nd she had greatly improved and was removed from a private ward to the ordinary ward. She was almost free from choreic movements, her mind was clear, and her speech was much better. The bruit was almost gone from the pulmonary artery. There was still a double bruit at the apex, but this was less marked; there was also a slight presystolic thrill. On the 23rd she was ordered five minims of arsenical solution three times daily. On the 28th she was able to feed herself and was taking 40 grains of chloralamide in the 24 hours. She was able on the 29th to thread a needle and to write her name fairly well. On the 30th the chloralamide was omitted and on Jan. 20th, 1903, she was discharged cured and with no choreic movements. Since her discharge she has attended at the infirmary occasionally as an out-patient. She continues well but there are some hypertrophy of the heart and some mitral incompetence.

When the patient was transferred to my care she was certainly in a very critical condition and in the opinion of both Dr. Barrs and myself the indications were strong for terminating the pregnancy. The chorea of pregnancy depends upon a condition of toxæmia. The pregnant state fosters the toxæmic condition and renders it very little amenable to treatment by drugs. To terminate the pregnancy seems a rational method of treatment. Its effect cannot be expected to be instantaneous but may develop in two or three days. The logical demonstration of the effect of inducing delivery is impaired by the fact that chloralamide was given, and given with obvious benefit, on Dec. 15th and onwards. In my opinion the improvement began before this and the patient, who had previously derived no apparent good from drug treatment, now benefited at once. At the same time I admit that chloralamide had not been tried before delivery. Still chloral and bromide had been pushed to the full and the patient was getting worse. There is practically no doubt that inducing abortion saved her life.

Chorea gravidarum is not an essentially incurable disease. Mild cases occur from time to time which clear up without serious trouble and even marked cases may recover and go to full term, but it is a very serious complication of pregnancy and if the mortality is not so high as was formerly estimated—as by Dr. Barnes who found 20 deaths in 68 cases (29·4 per cent.)—it is still very high. Buist estimates it at 17·5 per cent., Kroner at 22 per cent., and Spiegelberg² at 26·9 per cent. The presence of endocarditis, as in this case, is a serious factor in prognosis. No one suggests that artificial delivery is the routine treatment for all cases, but it is the treatment to be applied when chorea gravidarum threatens life. When the movements are slight, when the patient can eat and sleep well and maintains her weight, when the pulse is under 100 and there is no pyrexia, or when confinement to bed suffices to keep the patient fairly quiet and comfortable, then there are no indications for radical measures. When, on the other hand, the movements are violent and continue so in spite of rest in bed and drug treatment, when the patient cannot sleep or take food enough and is losing weight, when the mental condition is confused and there is a tendency to delirium, when there are a rise of temperature and a dry tongue, and especially when the pulse is persistently above 100 and is becoming weaker and more rapid, then the indications are complete and absolute. One thing more, however, must be said. If we wait for indications as complete and absolute as these we may find that we have waited too long. The attempt to save the foetus may lose the patient. In chorea gravidarum, as in hyperemesis gravidarum, the cases which require interference require it in good time. In my next case I shall

not wait so long as I did in the one under consideration.

As a matter of technique I greatly prefer in such a case induction of abortion by stimulating the physiological action of the uterus to a forced mechanical delivery at one sitting. Some mechanical dilatation may be useful to complete delivery, but a preliminary setting up of uterine action by the bougie is of great advantage. The fact that we have now powerful rapid mechanical dilators available does not alter this opinion.

Leeds.

A SIMPLE EXPEDIENT IN THE ESTIMATION OF SUGAR BY THE COPPER REDUCTION METHOD.

By S. ARCHIBALD VASEY, F.I.C., F.C.S.

FROM time to time the original method devised by Fehling for the estimation of sugar has been modified in some way or other, chiefly with the view of making the end of the reduction process more accurately and easily observable. It is probable that accuracy is more likely to ensue when the reagents are kept as near simplicity as possible. The modifications of Fehling's original processes have consisted in the addition of reagents in which the reduced copper is soluble, so that the blue colour is discharged by the addition of the sugar solution, a clear colourless solution being finally obtained. Thus Pavy suggested adding strong ammonia and Gerrard cyanide of potassium to the Fehling mixture. Both modifications present advantages when operating upon certain fluids with sugary contents. Pavy's method works well and gives accurate results for all ordinary purposes in the case of estimating milk sugar directly in milk or glucose in urine, but the results are variable according to the ammoniacal strength of the copper solution, and it is hardly possible to keep this constant, since the solution must be used boiling. Then the ammonia fumes are troublesome. Gerrard's cyanide process has no objections of this kind but it is somewhat complicated and involves the employment of a solution of potassium cyanide which is not stable. The process, however, is accurate.

As is well known, the drawback to the original method of Fehling is the formation and suspension of red cuprous oxide in a blue solution. The oxide is so fine that it is slow to separate and to agglomerate and thus it is difficult to mark exactly when all trace of the blue colour has disappeared or, in other words, when the whole of the copper is in the insoluble condition of cuprous oxide. It occurred to me that instead of adding a reagent to form a soluble compound with the cuprous oxide as it is produced, as in Pavy's and Gerrard's processes, an inert powder, preferably of a clear white colour, might be employed so as to entangle the precipitated oxide and carry it rapidly to the bottom of the solution and thus to leave a clear liquid above in which the faintest trace of blue could be seen. I subsequently found that precipitated chalk and later barium sulphate fulfilled this idea admirably. Lead or aluminium salts are obviously inadmissible. I now proceed as follows. To the measured quantity of Fehling's solution (generally ten cubic centimetres) suitably diluted I add about two teaspoonfuls of finely precipitated calcium carbonate or barium sulphate. The mixture is then raised to the boiling point, being gently stirred with a glass rod during the whole time. The solution in which the amount of sugar is required to be known is then run in after the usual manner. It will be found that the red cuprous oxide will be deposited upon, and evenly distributed through, the chalk slime or the barium sulphate which rapidly subsides, so that the true colour of the clarified supernatant liquid is quite easily seen. In this way the exact point of transition from a trace of blue colour to a colourless solution can be sharply noted. The process is rapid and extremely accurate according to a number of estimations made by me with standard solutions of sugar, diabetic urines, wines, and other sugary fluids, and it certainly has the merit of simplicity. This modification I feel sure will be found to be very convenient in clinical practice.

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² See article by Hirsche in the *Monatsschrift für Geburtshilfe und Gynäkologie*, January, 1903. (An abstract of this article appears in the *Journal of Obstetrics and Gynaecology*, April, 1903.)

PRELIMINARY NOTE ON THE USE OF CHLOROFORM IN THE PREPARATION OF VACCINE.¹

By ALAN B. GREEN, M.A., M.D. CANTAB.

(From the Government Lymph Laboratories.)

It is well known that glycerine exerts an action on vaccine whereby the extraneous bacteria are eliminated in the course of a few weeks, while the specific germ undergoes no undue deterioration from the process. I have found that by the use of a solution of chloroform in distilled water the extraneous bacteria of vaccine are eliminated in from one to six hours, the specific germ remaining fully potent for vaccination. The solution of chloroform that can most advantageously be employed in the preparation of vaccine is a saturated solution in distilled water, having a strength of 1 in 200. This is the limit of such solubility.

The following method of using such solution has so far given the best results. Vaccine emulsion is first prepared by triturating vaccine pulp with distilled water. *The presence of the water is essential* in order that later chloroform may enter into solution with it. About three parts by weight of water should be mixed with one part by weight of pulp. Should a more viscid emulsion of vaccine be desired glycerine may be added without interfering with the action of the chloroform. I have found that the usual admixture of one part by weight of vaccine pulp and four parts by weight of a solution consisting of equal parts by weight of glycerine and water forms a perfectly suitable emulsion for this process. But glycerine is incapable of dissolving chloroform and the elimination of extraneous bacteria by this chloroform process is solely due to the action of chloroform water. Indeed, when the addition of glycerine to the vaccine emulsion is desired, it can be very advantageously effected after the completion of the process. The newly made vaccine emulsion to be subjected to the action of chloroform is dealt with in the following way. Sterile air is first passed through pure liquid chloroform, whereby this air becomes charged with chloroform vapour. This mixture of air and chloroform vapour is then passed through the vaccine emulsion, which is contained in a cylindrical glass vessel of test tube shape and in size suitable to the quantity of vaccine to be treated. The mixed chloroform vapour and air can be passed seriatim through a number of tubes of vaccine before it finally escapes into the outside air, and it is efficient for all of them, provided that the current be sufficiently strong to keep the contents of each tube in active movement, and that a distinct smell of chloroform be apparent at the outlet of the last tube of the series. It is essential that no liquid chloroform be allowed to pass over into the vaccine, as its presence is strongly inimical to the potency of the lymph. To obviate the chance of such an accident an overflow bottle, weighted with sterile sand, is interposed between the bottle of liquid chloroform and the tube or tubes of vaccine emulsion. By passage through it of chloroform vapour and air the water of the vaccine emulsion quickly becomes saturated with chloroform and this strength of solution is maintained so long as such passage is continued. When saturation is reached all excess of chloroform immediately escapes automatically from the vaccine. Thus the vaccine is not at any time brought into contact with a stronger solution of chloroform than 1 in 200 in water.

A rapid and marked germicidal action is exerted on the non-spore-bearing extraneous bacteria of vaccine thus treated. The extraneous bacteria most commonly found in vaccines at the Government laboratories are staphylococcus pyogenes aureus, staphylococcus pyogenes albus, staphylococcus cereus flavus, and staphylococcus cereus albus. Others which occur either in smaller numbers or less commonly are staphylococcus pyogenes citreus, proteus vulgaris, streptococcus pyogenes, sarcina lutea, and some yeasts. Emulsions which have contained as many as 100,000 extraneous micro-organisms per platinum loopful at the time of mixture have, by the action of chloroform water, become free from their presence in from one hour to six hours. This

freedom is evidenced by absence of bacterial growth in aerobic and anaerobic plate cultures. The germicidal action is first exerted on the least resistant members of each species of organism present in the vaccine. Generally after the first hour or one and a half hours of the process a very few of the more resistant staphylococci—*aureus* and *albus*—remain alive; these give rise to small inhibited colonies in plate cultures and these organisms succumb in their turn after further application of the process.

By contrast, elimination in like degree of the extraneous micro-organisms of vaccine by the glycerine process rarely occurs before the fourth week after mixture and is frequently not complete until a much later period, as shown by similar plate cultures. After elimination of extraneous bacteria from chloroformed vaccines the chloroform is evaporated until no trace remains. Such evaporation is most quickly effected by passing a stream of sterile air through the emulsion.

By the above method vaccine can be brought under the influence of the germicide for such time only as suffices to kill the extraneous micro-organisms. At present, however, there is no evidence to show that more prolonged contact with 1 in 200 watery chloroform solution has any harmful effect on its potency. As in the case of glycerine, non-spore-bearing bacteria in vaccine lymph are alone killed by this process. But in some thousands of vaccines examined at the Government Lymph Laboratories the only spore-bearing organisms found in vaccine were the strictly non-pathogenic organisms of the mesenteric group—*bacillus mesentericus vulgatus*, *bacillus mesentericus fuscus*, *bacillus mesentericus ruber*, and *bacillus subtilis*—and equally non-pathogenic moulds such as *penicillium glaucum*.

The practical working value of the foregoing method has been clearly shown by results of vaccinations performed with vaccines which have been thus subjected to the action of chloroform. These vaccines, having been rendered free from extraneous micro-organisms, were first tested on calves and were found to give excellent results. Within a fortnight after collection from the calf and of subjection to the action of chloroform water, such vaccines have been used (after evaporation from them of all chloroform) for primary vaccinations and revaccinations with results of high "case" and "insertion" success. It would seem, therefore, that the following considerable advantages are to be gained by the use of the chloroform process:—

1. So speedy an elimination of extraneous micro-organisms is attained that vaccine, practically free from such organisms, can be distributed for use within a few hours of its collection from the calf. In times of urgent demand for large quantities of vaccine, such as occur during small-pox epidemics, this process must needs prove of great value, since the necessity for wasting some weeks for elimination of extraneous organisms by glycerine will be done away with.

2. In so far as the vaccination value of vaccine depends on the activity of a living organism deterioration of that value must occur in the course of a longer or shorter time. The potency of some vaccines, glycerinated or otherwise, becomes greatly impaired within a few weeks of collection—that is, within the time required for glycerine to exert fully its influence in eliminating extraneous organisms. Some of these vaccines may, at the time of their collection, have possessed a high vaccination value. Vaccine, characterised by this high but somewhat transient potency, can by means of the chloroform process be used at once before its activity has deteriorated, thus allowing greater economy of vaccine material than would otherwise be possible.

3. For a similar reason the chloroform process might be of considerable use in hot climates where the preservation of the potency of vaccine is frequently a matter of considerable difficulty.

Experiments are at present being made to test the duration of the potency of chloroformed vaccines. A further account of this process will be given in the report for 1902-03 of the medical officer of the Local Government Board.

In conclusion, I wish to express my indebtedness and thanks to Dr. F. R. Blaxall for the generous help and advice which he has given me. My thanks are likewise due to Mr. H. S. Fremlin, with whom I am also associated in the work of these laboratories, and to Mr. S. D. Rowland of the Jenner Institute of Preventive Medicine for help afforded me.

¹ A paper read before the Royal Society on April 30th, 1903.