The value of Carrel-Dakin's solution for irrigation has already been referred to. One of the causes of chronic empyema is the organization of lymph so that it forms a sheath over the lung, preventing its re-expansion. Unless the visceral pleura is sufficiently supple reapposition with the parietal pleura cannot take place. If, on the other hand, the cause of incomplete expansion of the lung is due to fibrotic changes in the lung itself, approximation of the pleural membranes may still be possible owing to displacement of the mediastinum. Dakin's solution, by virtue of its solvent action, can often so free the pathological deposit from the pleura that the lung is again mobilized and capable of re-expansion. This action of Dakin's solution may liberate the plug closing a bronchial fistula, the existence of which was unknown. In such a case the use of the solution must be discontinued on account of the irritating cough it produces, and the risk of inspiration into the lung.

It is sometimes difficult to decide when to remove the drainage tube. A tube left in too long is apt to be responsible for a chronic sinus. This, unless of long standing, will clear up by the simple expedient of taking the tube out. A drainage tube is a source of irritation and therefore of reinfection, and must be removed as early as possible. The indication is the character of the discharge and the re-expansion of the lung as shown by *x* rays. If the lung is showing itself capable of expanding again, the tube should be omitted as soon as the discharge has ceased to be purulent, and is sterile.

It is essential from start to finish to treat the wound and empyema cavity with every aseptic precaution. A patient discharged from hospital while there is still a cavity or a sinus may, for the want of an additional week or two weeks' rigid supervision and care, be condemned to further operations, or to years of drainage, or even to a premature death from chronic sepsis or cerebral abscess.

DIET AND EXERCISES

The importance of nutrition was indicated by Bell of the Empyema Commission. He found that unless the diet contained a large amount of calories a day (from 3,300 to 3,500), an adverse nitrogen balance was produced, which meant a serious loss of weight. Graham recommends lactose, which is easily disguised by fruit juices, and also the subcutaneous administration of a 2 to 3 per cent. solution of glucose. Water should be given in considerable quantities during the febrile stage.

After the acute phase is over, breathing and blowing exercises should be started to increase the inflation and expansion of the lung so as to aid in the obliteration of the cavity.

CHRONIC EMPYEMA

The causes of chronicity can be divided into two groups—(a) cases in which chronic empyema could have been prevented, and (b) cases in which healing is very difficult owing to the primary cause or to unavoidable complication. The first group unfortunately is considerably the larger. It includes empyemata either not recognized or not treated until the pleura has become a rigid membrane by organization changes; those in which drainage has been inefficient owing to the opening being too high or too small; those in which reinfection has occurred; those in which irrigation with Dakin's solution has not been done and was necessary to remove the deposited lymph in order to prevent organization or to arrest persistent infection. Finally in this group of preventable cases are those in which the chronic cavity is maintained by the presence of a foreign body, such as a drainage tube, or fragments of rib, or on account of osteomyelitis of the divided rib.

The second group, in which the chronic empyema is due to unavoidable complications, includes those cases with bronchial fistula, with associated fibrosis of the lung, or in which the primary cause was tuberculosis or actinomycosis.

The first line of treatment is directed to rectify, when possible, the original fault. Efficient and dependent drainage must be instituted, preferably by enlarging and extending the original opening, if that is practicable; if not, by making a new opening. Foreign bodies should be looked for and removed. Frequent irrigation with Dakin's solution will help to sterilize the cavity and may even effect a decortication of the pleural surface, separating off the organized lymph. Dakin's solution should not be used, however, if the case is tuberculous, or, as has previously been stated, if there is a bronchial fistula.

It is only when these measures have been given a full trial that the major operative procedures are indicated. The object of these is to mobilize the chest wall by denuding it of the ribs over the affected area, and at the same time mobilizing the lung by decortication—that is, stripping the organized lymph off the lung and pleura. When dealing with a cavity of any size, mobilization of the chest wall alone or of the lung alone is rarely adequate. The operations must be performed in a series of stages, and it is most important that approximation should start at the apex and that apposition should be secured over the upper area before an attempt is made to obliterate the lower segment. In cases of very large empyemata it may be necessary to dissect away the whole of the parietal pleura, together with the periosteum of the ribs and the intercostal muscles.

Bronchial fistulae may clear up spontaneously after free drainage has been instituted. If not, the opening should be cauterized. To obliterate a large chronic fistula the bronchus must be freed, the end cauterized and closed by sutures, and the lung mobilized so as to bring it into apposition with the chest wall.

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THE EFFICIENCY OF ANTISEPTICS USED IN MIDWIFERY

BY

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Early last year it was pointed out in the correspondence columns of the *British Medical Journal*¹ that doubts had been raised of the utility of lysol as an antiseptic for obstetric use. A memorandum circulated by the London County Council, and reissued by the Central Midwives Board, gave particulars of tests which indicated that only comparatively strong solutions of lysol were capable of killing *Streptococcus pyogenes*, and, further, that different brands of lysol varied considerably in their bactericidal potency. It was not unnaturally asked what antiseptic should be substituted for lysol in midwifery, and this question has not until now, so far as I am aware, received an answer, either in the medical press or in the pronouncement of any public health authority. Meanwhile the Central Midwives Board has recommended the continued use of lysol by midwives, provided that it conforms to a certain chemical standard—namely, a 50 per cent. cresol content.

To those familiar with the properties of germicides the use of lysol in obstetrics has always appeared mistaken. It is the most caustic of all antiseptics in clinical use, with the single exception of phenol, and the limitations imposed by this property on the strengths of solutions employable bring them dangerously near a point at which they are ineffective. There is therefore a *prima facie* case for inquiry into the suitability of other agents, but it may first be asked whether the use of a germicide as such—that is, with an expectation of destroying bacteria—is desirable or useful in midwifery. The ideal of some obstetricians is “asepsis,” and they do not apparently believe in the utility of any attempt to destroy bacteria by chemical means; if they use lysol it is for other reasons (though it is to be noted that the vast majority of practitioners regard lysol in the light of a safeguard against infection). Some colour has been lent to this view by the work of Colebrook,² who found that none of a number of germicides was capable of sterilizing the skin of hands artificially infected with streptococci.

Assuming that puerperal infection is exogenous, the question at issue is whether treatment of the vulva and vagina with an efficient germicide will or will not destroy streptococci which may gain entry to the birth canal during childbirth. Making every allowance for the difference between conditions *in vitro* and *in vivo*, there is strong presumptive evidence that such an action can be exerted. If chemical prophylaxis is a myth, why do obstetricians themselves instil silver nitrate solution into the conjunctiva to prevent ophthalmia neonatorum? To take an example from the vagina itself, has anyone ever disputed the efficacy of the mercury and silver preparations issued to troops during the war for the prophylaxis of syphilis and gonorrhoea? And, as a third example, who has ever heard of a surgeon during the last forty years opening an abdomen without first attempting to sterilize the skin, again by chemical means? It is a common-sense view that prophylaxis is the really useful sphere of germicides. Their utility in established infections is more doubtful, although they are employed for treating septic wounds, and are even injected into the blood stream in septicaemia; but to kill a streptococcus before it has gained access to the tissues, to erect a barrier through which it cannot pass alive, is surely not an impossible thing. If a germicide cannot do this it can do nothing.

The success of measures hitherto adopted for reducing the persistently high mortality from puerperal sepsis has not been such as to permit the neglect of any measure reasonably calculated to assist in attaining this object. It is therefore submitted that an antiseptic technique aimed at prophylaxis is worthy of extensive trial, and the experiments to be described were designed to determine what agent is likely to be most efficient for this purpose. It is a common practice to decry *in vitro* tests of germicides as unreliable indicators of activity *in vivo*, and however laboratory conditions may be modified to imitate clinical conditions, no one would care to rely for clinical purposes on the maximum dilution found to be effective in the laboratory. Often, however, it is possible to use for clinical purposes considerably stronger solutions, and in any case the same consideration applies to all the agents tested: the most active under appropriate conditions *in vitro* may reasonably be assumed to be the most active *in vivo*.

It is not sufficiently well known that the action of any germicide may differ widely with different bacteria. The statement of a Rideal-Walker coefficient, the only evidence (if any) usually adduced of the activity of a germicide, refers to its action on *B. typhosus*; for a streptococcus its lethal activity may be greater or less to a considerable degree. It is therefore important, when considering germi-

cides in relation to any given lesion, to possess comparable data concerning their action on the micro-organism causing that lesion. A strict comparison is only possible if all have been tested under the same conditions. The organism used in the present investigation was *Strep. pyogenes*, which is unquestionably responsible for almost all fatal and the majority of other grave cases of puerperal infection.

METHOD OF TESTING

Each germicide was tested in four ways. The bactericidal action (that is, the ability to destroy the streptococcus in a given time) was studied under two conditions: in a medium of distilled water with no added organic matter, and in the presence of a proportion of added blood at the temperature of the body. The bacteriostatic action (that is, the ability to prevent growth without necessarily destroying) was studied also under two conditions—namely, in media containing no protein, and in media containing blood. The use of blood as added organic matter appears justified by the conditions in which a germicide is used in obstetrics; the material with which it will chiefly be mixed when its presence is designed to prevent the access of bacteria to the placental site or a cervical laceration, is blood. Serum, which has often been used, appears less appropriate to the purpose here in view, and such materials as milk, urine, sterilized faeces, etc., are clearly less applicable.

The following are details of the technique employed:

A single strain of *Strep. pyogenes* was used throughout; its origin, which was recent, was blood culture from a rapidly fatal case of septicaemia following abortion. The preparation used for tests was not the usual broth culture, but a suspension of a strength of at least 1,000 million per c.cm. prepared by emulsifying a twenty-four-hour blood-agar plate in saline, and treatment in a mechanical shaker. Broth was avoided in order to exclude extraneous organic matter completely, and the object of shaking was to break down clumps of cocci, the presence of which, owing to failure of penetration by the germicide, may undoubtedly vitiate results with this organism. For the purpose of tests in the first category, two drops as delivered by a small separating funnel (equivalent to slightly less than 0.1 c.cm.) of this emulsion were added at timed intervals to a range of tubes containing approximately 4 c.cm. each of a range of dilutions of the germicide; these were shaken and left at room temperature; cultures were made after fifteen minutes, a 2 mm. loopful being sown in blood broth. The presence or absence of growth in the cultures was noted after forty-eight hours.

The dilutions used rose by 50's from 100 to 500, by 100's to 1,000, by 200's to 2,000, by 500's to 5,000, by 1,000's to 10,000, and thence as multiples of the foregoing.

In the tests of bactericidal action at 37° C. in the presence of blood, the dilutions of the germicide were reduced to a volume of 4.5 c.cm. in tubes graduated for this purpose, which were placed in racks in a water-bath at 37°. After the contents of the tubes had reached that temperature each received 0.5 c.cm. of a mixture of equal volumes of sterile defibrinated blood and saline emulsion of streptococci (in one series of experiments citrated blood was used). Each tube thus contained an amount of blood equivalent to 5 per cent. of the total volume of fluid. The tubes were shaken, kept in the bath for fifteen minutes, and then cultivated in the same manner as the others. It was originally intended to prepare dilutions of such strength that the addition of 0.5 c.cm. would bring them to the dilutions used in the foregoing series of experiments. It was found more convenient, however, to use the same actual solutions for both, and the dilutions in this series have therefore to be corrected for the addition.

For the tests of bacteriostatic action 500 c.cm. double strength peptone broth was made up to 800 c.cm. and tubed in 4 c.cm. amounts; to each was added 1 c.cm. of a dilution of the germicide, the dilution in the resulting mixture with the medium being thus five times greater, and the concentration of the other ingredients correct. These tubes, with or without added blood, were inoculated and read after forty-eight hours. Owing to difficulty in observing whether growth had occurred

in some of the cultures containing blood, several of these experiments were done using tubes of 4 c.cm. agar, which were sloped and surface-sown. Parallel experiments using both media showed that the results given by the two were identical.

Many of the experiments were done several times, either because a wrong range of dilutions had originally been used, to confirm unexpected results, or to reconcile conflicting results. Some of the figures given represent averages of the results of several experiments; it is admittedly impossible to attain perfect consistency in repeated experiments of this kind.

A word of explanation is necessary for the procedure of cultivation, after exposure to the action of the germicide, in blood broth. It had been observed by the writer some years ago that the use of this medium rather than plain broth reduced the apparent efficiency of a germicide for streptococci as much as twenty-five-fold. It appeared that exposure to weak solutions reduced their vitality, with the result that they failed to grow in a poor medium, but grew readily if it were enriched by blood. This observation was fully confirmed in this series of experiments. In some of them, cultures after the fifteen minutes' exposure were made in both media with greatly contrasted results. Thus the apparent maximum effective dilutions, as indicated by subsequent growth in the two media, were as follows:

	Broth.	Blood Broth.
*Mercury perchloride...	1: 10,000	1: 250
Brilliant green ...	1: 25,000	1: 4,000
Acridiflavine ...	1: 2,500	1: 900

That this phenomenon is not peculiar to streptococci is shown by the fact that similar results were obtained with mercury perchloride and *B. coli*. Other experiments indicate that the cells rather than the plasma contain what may be called the growth-stimulating factor. The nature of this phenomenon is being made the subject of a separate investigation. All the figures given in the tables represent the results of cultivating in blood broth, which, as will have been seen, is the severer test of bactericidal action.

DISCUSSION OF RESULTS

Table I gives the whole of the results in figures;

TABLE I.

	1	2	3	4
	Maximum Bactericidal Dilution in 15 min. in distilled water at room temperature	Maximum Bactericidal Dilution in 15 min. at 37° C in the presence of 5 per cent. of blood*	Maximum Dilution in culture inhibiting growth in peptone broth	Maximum Dilution in culture inhibiting growth in peptone broth + blood
	1 in	1 in	1 in	1 in
Phenol ...	100	150	400	500
Eusol ...	500	2	5	<5
Mercury biniodide	50	100		
Mercury perchloride	250	400	50,000	12,500
Lysol 1 ...	600	300	4,000	1,500
" 2 ...	450	300	2,000	1,000
" 3 ...	1,600	500	6,000	2,000
" 4 ...	600	300	6,000	1,000
Cyllin (medical) ...	2,000	1,800	5,000	5,000
Izal ...	3,000	800	5,000	2,000
Monsol ...	700	1,200	10,000	5,000
Acridiflavine ...	900	500	1,250,000	1,250,000
Rivanol ...	400	600	200,000	200,000
Brilliant green ...	4,000	10,000	1,250,000	30,000
Mercurochrome ...	<100	<100	12,500	500

* Figures in this column, for strict accuracy, require a correction of + 11 per cent. for the volume of blood and bacterial suspension added.

Table II represents the more important of them diagrammatically. The scale of this diagram is logarithmic, with

* Cultures made in broth containing ammonium sulphide gave similar results to those in plain broth.

the dilution 1 in 100 as zero; the maximum bactericidal and bacteriostatic dilutions are represented in the case of each germicide, the figures used being those in the second and fourth columns of the table. Emphasis is thus laid

TABLE II.—Comparative Efficiencies of Seven Germicides Tested
(See Columns 2 and 4 of Table I)

on bactericidal action at 37° in the presence of blood and on bacteriostasis in blood-containing media, because it is believed that these conditions more truly represent those which obtain in clinical use. It is noteworthy that two factors are concerned in the former, which account for differences between the results and those of ordinary tests at room temperature without organic matter (Column 1 of Table I): the higher temperature, which usually intensifies bactericidal action; and the presence of blood, which often diminishes it. The varying effects of these two factors combined are interesting.

Some of the results call for brief individual comments.

Eusol.—The contrast between the effective bactericidal strength of eusol in distilled water and its behaviour in the presence of blood, or even peptone broth, is striking and familiar. It cannot be emphasized too strongly that agents of this class are worthless in the presence of any considerable amount of organic matter.

Mercury Salts.—The effect on the results obtained with these agents of cultivating in blood broth has already been discussed; this method shows that mercury salts have considerably less bactericidal power than is usually supposed. Somewhat surprisingly, they are effective in greater dilution at 37° C. in the presence of 5 per cent. of blood than in distilled water at room temperature. Of the two, the biniodide is much the weaker, but according to these results neither can be effective in the dilutions used clinically.

Lysols.—Lysol 1 is the original German lysol (Schulke and Mayr); the other three are well-known brands sold in England, all having a guaranteed 50 per cent. cresol content. Their bactericidal power varies; one is somewhat inferior to its foreign prototype, one decidedly superior, and one identical. Excluding from consideration No. 3, which clearly must contain different cresols from the remainder, the maximum effective bactericidal concentration under clinical conditions is 1 in 300. The strength of No. 2 recommended for use in the vagina is 1 in 400. This lysol therefore fails. It is equally clear that the use of any lysol, even in somewhat stronger solution, can leave very little margin of safety.

Cyllin, Izal, and Monsol.—These are proprietary germicides of coal-tar origin, all of which form an emulsion, as distinct from a solution, when diluted in water. Their average efficiency is much greater than that of lysol. A comparison between their action in distilled water and in 5 per cent. blood at 37° C. is interesting: cyllin appears almost equally effective in

either condition; izar is better under the former, and monsol under the latter. These germicides are less poisonous than lysol and less irritating to the skin, despite their much greater efficiency. They can, however, presumably be irritating in the vagina, since the strengths recommended for use are respectively 1 in 600, 1 in 600, and 1 in 500 (increased). Even in these weak dilutions there is a clear margin of safety.

Acriflavine and Rivanol.—These may be considered together, since they are compounds of somewhat similar composition, and they share the property of exerting a bacteriostatic action in enormous dilutions, whereas their bactericidal power in short periods of time is comparatively feeble. The former action is in both cases unaffected by blood. The bactericidal power of acriflavine is somewhat diminished by the presence of blood: this contrasts with the statement that it is actually enhanced by the presence of serum (Browning).³

Brilliant Green.—It may be said at once that brilliant green emerges from this investigation as by far the most potent of all the substances tested. The fact that it destroys *Strep. pyogenes* even in the presence of blood at a dilution of 1 in 10,000 becomes even more striking and significant when it is remembered that even strong solutions are without irritant action. In "blue paint" (Bonney and Browning)⁴, which has now been used for obstetric and other purposes for fifteen years, its concentration is 1 in 200. It is thus practicable to employ a solution of fifty times the strength demanded for rapid bactericidal action.

Mercurochrome.—It is evident from the results in Table I that mercurochrome (of which two makes were tested) is a germicide incomparably weaker than is commonly supposed. Others have obtained similarly unsatisfactory results with it (Simmons,⁵ Ramos,⁶ Walker⁷), and an explanation of the discrepancy between these results and those of Young, who introduced the drug, has been suggested elsewhere (Garrod).⁸ A solution of a strength of no less than 1 in 25 has, however, been said to reduce the incidence of puerperal sepsis (Mayes).⁹

COMMENTARY

In drawing practical conclusions from these results it is necessary first to decide whether the purposes of obstetric prophylaxis can be served by merely bacteriostatic action; if this be so, acriflavine is the most powerful agent we possess. In order that this action should be effective, an adequate concentration would presumably have to be maintained in the birth canal for several days, immobilizing any streptococci which might gain entrance, until the states of the placental site and the cervical laceration were such that bacterial invasion could no longer readily take place. That a rapid bactericidal action, if obtainable, is preferable to this, must be obvious.

Of the germicides tested, few possess a bactericidal action on *Strep. pyogenes* which appears adequate. The meaning of the chief results may be concisely stated by calculating the ratio of effective strength to strength employed, which may be termed the factor of safety. Taking the figures in Column 2 as the effective bactericidal strength, the factor of safety for brilliant green is 50, for cyllin 3, for lysol 0.75, for mercury biniodide 0.1. The contrast thus afforded between two effective and two ineffective agents is sufficiently striking.

There is no doubt that brilliant green is by far the surest safeguard against streptococcal infection which can be used; it would be interesting to know whether grave sepsis has ever been seen to follow its employment. It is objected to on account of its staining propensities; whether stained linen or death from septicaemia is the

greater evil is a question which seems to admit of only one answer. Next in order of efficiency come the proprietary coal-tar germicides, monsol, izar, and cyllin; these are sometimes objected to on account of their smell. Acriflavine, rivanol, and one brand of lysol are on the borderline of bactericidal efficiency; other lysols, mercurochrome, and mercury salts are ineffective.

The purpose of this paper is to indicate which germicides may be expected to prevent streptococcal infection during childbirth: the method of their application is outside its scope. That a technique can be devised which would ensure their effective action is hardly doubtful.

CONCLUSIONS

1. The bactericidal and bacteriostatic action of fifteen germicides used in obstetrics have been tested, the test organism being *Strep. pyogenes*, and the conditions employed such as to imitate as far as possible those of obstetric use.

2. Four of the germicides tested are calculated to be effective in the dilutions employed clinically, one, brilliant green, affording a very wide margin of safety; of three the efficiency is doubtful; the remaining eight are judged to be untrustworthy.

This work was carried out during the tenure of a grant for work on streptococci from the Medical Research Council, to whom I express my thanks, and to my assistant, Miss G. E. Root, for assiduous help in the laborious work involved.

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THALLIUM ACETATE IN TREATMENT OF RINGWORM OF THE SCALP

A STATISTICAL INVESTIGATION OF SUBSEQUENT NUTRITION

BY

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Since November, 1928, 139 children suffering from ringworm of the scalp have received an epilating dose of thallium acetate at the skin department, Royal Infirmary, Edinburgh. The dosage employed was 8.5 milligrams of thallium acetate per kilogram of body weight; this was administered to children weighing up to 33 kilos. The treatment has been successfully completed in 122 of these cases, the remaining 17 being still under supervision. During the same period only 29 children suffering from ringworm of the scalp have received an epilating dose of x rays. From a survey of the cases treated with thallium acetate it seems that the immediate results of this method of treatment are on the whole superior to those obtained in cases treated by x rays.

ADVANTAGES AND DISADVANTAGES OF THALLIUM

Thallium is easily and rapidly administered. On account of this a large number of children can be dealt with in a very short time, whereas an epilating dose of x rays for the entire scalp takes at least an hour to administer,

* In receipt of a grant from the Medical Research Council.