of cardinal importance; and in countries like Holland, Sweden, and Australia, and in great towns like Amsterdam and Chicago, which now lead the world in their low infant death rates, special attention has been paid to the training of health nurses. In the light of these facts, the curriculum and the training of our health visitors must be drastically overhauled and improved. With the better training of the nurse we must also have better training for the family doctor and the welfare clinic medical officer. That work of training seems to lie in the hands of the physicians in the teaching children's hospitals; but they must be given the clinical material for study and the facilities for teaching.

A perfect sanitary system alone cannot achieve a low infant death rate. To it must be added good obstetrics, which includes the skilled care of the mother before and during birth and the care of the infant and instruction of the mother after birth, which make up good paediatrics. We may justly claim that our obstetrics is good, and that by study and teaching a constant effort is being made to improve it. But in comparing our infant death rates with those of countries like Holland and others we must admit that our preventive paediatrics is second-rate. A reduction of infant death rates in England and Scotland to the forties and thirties is not likely to come about by better drains and better houses, or by multiplication of our child welfare clinics and health visitors. For a further substantial reduction in infant deaths the first requirement is that those who teach the mother how to protect the health of her baby must themselves be taught and trained in these protective techniques in our medical schools.

THE TREATMENT OF PHOSPHORUS BURNS

BY

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AND

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Our attention has been drawn by Major Roland Heath, commanding officer of the Northwood, Middlesex, Home Guard, to the lack of adequate first-aid treatment of phosphorus burns. As the incidence of these burns may be considerable if hostilities extend to this country, the subject is obviously of great importance. Major-General T. S. Coates (1941) gives the following description of the official method of treatment, which is obviously unsuitable for first-aid application:

"1. Wash the burn immediately with a solution of sodium carbonate (2 tablespoonfuls to a pint of water). This treatment neutralizes any phosphoric acid formed as the result of the combustion of phosphorus, and partially destroys any free phosphorus present.

2. To free the burn from all traces of phosphorus, wash with 1% solution copper sulphate. Copper sulphate combines with free phosphorus, forming copper phosphide, thus preventing further ignition.

3. Remove the resulting dark-coloured deposit with forceps, and thoroughly wash with water containing a little antiseptic.

For extensive burns requiring hospital treatment, ultra-violet radiation is recommended and dressings of picric acid, etc., as for ordinary burns. Phosphorus burns suppurate much more than ordinary burns, and the healing period is usually three to four weeks."

We thought that it would be possible to replace the copper sulphate and alkali solutions with powders to be carried in small sifter containers from which they could be sprinkled on to the wound and worked up to a paste

with water from the water-bottle. Eventually a powder was obtained which appeared to form a suitable substitute for the alkaline solution; but, to replace the aqueous copper sulphate, a concentrated glycerin paste was found to have advantages over the powder preparations that were tried.

The greatest experimental difficulty was to obtain for treatment material similar to human phosphorus burns, the best available substitute being burns produced on shaved areas on the skins of rats recently killed in connexion with other experiments. The phosphorus-containing layer of an actual S.I.P. (self-igniting phosphorus) bomb was used as the source of phosphorus. This is referred to below as phosphorus liquid.

The experiments fell into three groups: (1) *in vitro* observations on the action of copper preparations of phosphorus liquid; (2) application of phosphorus liquid without ignition for varying periods of time to the skin of rats, and subsequent treatments; and (3) production of phosphorus burns on the skin of rats, and subsequent treatments. Small amounts (50 to 100 mg.) of the phosphorus liquid such as were often used in the following experiments do *not* ignite spontaneously unless the surface area is considerably increased.

Action of Cu Preparations on Phosphorus Liquid

Phosphorus Liquid with 1% Aqueous Copper Sulphate.—When a small globule of phosphorus liquid is rubbed up with 1% aqueous copper sulphate on a glazed tile very little action takes place. The liquid may be broken up into smaller globules and some brownish flakes may form at the interface, but the bulk of the phosphorus and copper sulphate fails to react. Further, chemical considerations indicate that the amount of copper which can be precipitated from solution by phosphorus is in the atomic ratio of at least 2Cu:1P (Mellor, 1928)—i.e., 1 part of phosphorus to approximately 16 parts of copper sulphate or 1,600 parts of the 1% solution. In other words, even if complete reaction took place $3\frac{1}{2}$ fl. oz. of the 1% solution would be required to destroy 1 grain of phosphorus.

Having regard to the adverse factors which exist in practice, it became obvious that a material of much higher concentration than the official solution would be required to effect a complete and rapid immobilization of even small quantities of phosphorus, whatever the precise method of application. This theoretical consideration appears to indicate one of the weaknesses of the official method.

Phosphorus Liquid and Copper Sulphate-Kaolin Mixtures.—The first powders tried were finely divided mixtures of copper sulphate and colloidal kaolin containing 5 to 50% of the former. The effect of these mixtures varied with the amount of water used in working up the liquid phosphorus with the powder. (It is important to notice that, in contact with any dry powder or fibrous material, such as paper, cloth, or cotton-wool, the phosphorus liquid ignites spontaneously owing to the exposure of a large surface by capillary action. *All treatments applied to a phosphorus burn must therefore be wet, so long as free phosphorus is present.*) When enough water was added to form a very thin cream the result did not differ greatly from that obtained with aqueous copper sulphate. A fairly stiff cream had a better effect in splitting the phosphorus globules, but reaction was slow unless considerable energy was used in grinding the materials together, and it was usually possible to observe globules of unchanged phosphorus by microscopical examination of the mixture.

Use of Emulsifying Agents.—A search for emulsifying agents capable of facilitating the break-up of phosphorus globules and thus exposing them to the more rapid action of the copper sulphate led to the following two formulas:

Formula 1			Formula 2		
Copper sulph.	..	50%	Copper sulph.	..	50%
Kaolin	..	45%	Kaolin	..	49%
Sulphonated lorol	..	5%	Sod. tauroglycocholate	..	1%

Each of these powders when stirred up to a moderately thick cream with phosphorus liquid gives an immediate emulsion in

which reaction, with the formation of a black coloration, rapidly takes place. *Provided sufficient copper sulphate is present and the mixing is thoroughly carried out, free phosphorus disappears completely in a few minutes.*

Paste Preparations of Copper Sulphate.—The view that a paste preparation of copper sulphate would be superior to a powder (a) because it might incorporate a hygroscopic material such as glycerin, which would avert the danger of drying before all the phosphorus had been destroyed, and (b) because the copper would be in solution and immediately available for reaction, led to the production and testing of a number of such preparations. The general results showed that when phosphorus liquid is rubbed up on a tile with a viscous liquid, such as a paste containing a high percentage of glycerin, a rapid mechanical emulsification is obtained. With a somewhat less viscous liquid containing an emulsifying agent, such as bile salts, there is equally good emulsification; while with still thinner products emulsification is poor. Emulsification is judged by microscopical examination or, if copper sulphate is present, by the formation, after keeping for a few minutes, of either a uniform brownish-black paste or one containing larger or smaller black specks, arising from undispersed globules of phosphorus. Mixing on a tile forms a more delicate test for emulsifying power than does, for instance, rubbing on the palm of the hand. Mixtures which show little emulsification in the former condition often give an immediate production of copper phosphide under the latter, owing possibly to higher temperature and friction. Glycerin has a particular advantage in its high solvent power for copper sulphate, and in spite of numerous trials no substitute of equal efficiency has as yet been found. For example, among hygroscopic agents, ethylene and propylene glycols are inferior to both glycerin and water as solvents for copper sulphate. Propylene glycol-water-copper sulphate solutions show no appreciable viscosity advantage over ordinary aqueous solutions. Syrups containing sodium lactate, sugar, or golden syrup had a good emulsifying action on the phosphorus, but were poor solvents for copper sulphate. Thin gels of starch or gelatin, which although highly viscous have little mechanical strength, have not the necessary "drag" and produce rather poor emulsification. Pastes containing copper hydroxide or carbonate react with phosphorus, but more slowly than copper sulphate solutions. They are open to the objection that more copper would be left in the tissues after treatment than would be the case with a soluble salt owing to the difficulty of washing the material away. The following formulas are recommended, the second being introduced as a slightly less efficient substitute in the interests of glycerin economy.

Formula 3

Copper sulph.	22.5%
Glycerin	67.5%
Starch	5.0%
Water	5.0%

Formula 4

Copper sulph.	20.0%
Glycerin	40.0%
Starch	7.5%
Sod. tauroglycocholate	1.0%
Water	31.5%

Liquid Phosphorus and the Alkaline Powder.—The alkaline powder (Formula 2A, below) was also found to have an excellent emulsifying action on phosphorus liquid, although the effect appeared to be entirely mechanical. This had an important bearing on the final method of treatment adopted.

Application of Phosphorus Liquid to Skins of recently killed Rats

When amounts of 50 to 100 mg. of phosphorus liquid are applied to shaved areas on the skins of recently killed rats they do not usually ignite, but undergo a slow atmospheric oxidation accompanied by phosphorescence. The material was left in contact with the skin for varying periods, so as to study the penetration of the phosphorus under more easily controlled conditions than in the case of an actual burn, and also to gain experience of the immobilization of larger quantities of un-ignited phosphorus than are found in an ordinary small burn.

Comparison of Solution and Powder Treatments.—In these experiments the phosphorus liquid was applied for varying periods, some of the rat skins being then treated by the official method and others with powders. In these tests we used the copper sulphate-kaolin mixtures already mentioned and alkaline powders composed of:

Formula 1A

Kaolin	42%
Sodium bicarbonate	42%
Borax	16%
with or without emulsifying agents, such as sulphonated lorol or bile salts.	

The results were such as would have been expected from the foregoing section. There was a tendency for the official solutions to displace phosphorus globules from the site of application without destroying them, whereas the powders kept the globules under better control. The most noteworthy effect observed, however, was the relative depths of penetration of the phosphorus and of the acid formed by its oxidation. After a few hours' contact with unignited phosphorus in air the skin was visibly altered, becoming stiffer and more translucent. After the appropriate period of application a piece of skin including the treated area was cut out, and tests were applied to the exposed surfaces to determine the degree of penetration. It was noticed that whilst a blackening with copper sulphate could be obtained only on the surface which had been in actual contact with the liquid, there was a steady penetration of acid, eventually extending through the skin to the subcutaneous tissues. The presence of acid was detected by observation of the effervescence on applying sodium bicarbonate, control tests being made on untreated areas of skin in the same animal. The results are shown in the following table:

Rat No.	Length of Application	Acid Present		Cut in S.C. Tissue
		Inside of Skin	Surface of S.C. Tissue	
1 & 2	$\frac{1}{2}$ hour	—	—	—
3	4 $\frac{1}{2}$ hours	+	+	—
4	9 "	+	+	?
5	24 "	++	++	++
6	32 "	++	++	++

These experiments were conducted with the skin at room temperature. It is reasonable to assume that the penetration would be more rapid at blood heat.

Note.—In an experiment in which the phosphorus was ignited and allowed to burn for two minutes there was immediate deep penetration of acid. Experiments of this kind are, however, difficult to control owing to the frequent occurrence of skin perforation.

It is concluded that in the official treatment not enough importance is attached to the removal of the deeply penetrating acid, and this indicates the second weakness of that method.

Production and Treatment of Phosphorus Burns on Skins of recently killed Rats

In forming the burns it was found convenient to confine the phosphorus liquid (50 to 100 mg.) within a metal ring (15 mm. in diameter) pressed tightly against the skin. This prevented the phosphorus from spreading and made the results more comparable. The phosphorus burned for one to two minutes and produced a second- or third-degree burn. The experiments were usually done in pairs, equal quantities of liquid being applied and allowed to burn for equal periods. The one burn was then treated by the official method and the other with the powders or paste, equal times of treatment being allowed.

The powders containing kaolin were found to be somewhat inconvenient to remove by subsequent washing. The copper sulphate powder was therefore replaced in our final experiments by the glycerin paste, and the alkaline powder by one composed as follows:

Formula 2A

Magnesium oxide, heavy	10%
Borax	5%
Sodium bicarbonate	85%

In addition to its good emulsifying power for phosphorus, this material is a free-flowing powder very suitable for use in a dredger. These advantages are given by the admixture of magnesium oxide, and both this substance and the borax confer a more alkaline reaction than sodium bicarbonate alone.

Finally, a test was made for free phosphorus in each burn, a convenient method being to dry the burn and then to rub the burnt area vigorously in a dark room, very small quantities of phosphorus rendering themselves visible by luminous flashes. Drying must be thorough (e.g., twenty minutes in a current of air at 40° C.) and rubbing must be persisted in for, say, three to four minutes before a negative result can be admitted.

The results, as expected, showed uniform and complete removal of free phosphorus when using the powder and paste; but when using the solutions, results were variable, and removal was often incomplete.

Proposals for the Treatment of Phosphorus Burns

As a result of the foregoing considerations we put forward the following rationale of treatment:

Stage I.—Remove the bulk of the free phosphorus and superficial acid with alkaline powder (Formula 2A). Under no circumstances must liquid suspected of containing phosphorus be dabbed with a handkerchief or other dry material. If water has been used to extinguish the phosphorus, sprinkle the powder on to the wet surface, add more water if necessary, and work up to a medium thick paste, covering the whole of the burn and the surrounding area if contamination is suspected. Wash or wipe off and reapply so long as marked effervescence continues. Drying must be avoided at this stage. The advantages claimed over the corresponding stage in the official treatment are: portability; greater concentration and osmotic effect (drawing acid products of combustion from the wound); and the prevention of displacement of unignited phosphorus to other parts of the body or clothes.

Stage II.—Immobilize the whole of the remaining free phosphorus by the use of glycerin-copper sulphate paste (Formula 3 or 4). Apply sparingly but thoroughly, and rub well in. Remove by washing or wiping as soon as no smell of phosphorus is perceptible in the wound. The advantages claimed over the same stage in the official treatment are: portability, concentration, rapidity, osmotic effect, and completeness of action.

Stage III.—Neutralize the deep-seated penetration of acid with alkaline powder (Formula 2A). Reapply the powder, work up to a paste with water, bandage, and dampen bandage occasionally. Do not allow bandages to dry. The importance of this stage has apparently not been previously recognized.

Stage IV.—Remove to hospital labelled "Phosphorus Burn."

Regarding subsequent hospital treatment we would suggest that all forms of coagulation therapy (tannic acid, picric acid, silver nitrate, etc.) be avoided in view of the obvious necessity for not "sealing in" the acid products. The very painful nature of phosphorus burns and the tendency to delayed healing may possibly result from the inadequate treatment of this acid concentration, and the alkalinity of the tissues may not be sufficient to deal with it. It is suggested, therefore, that continuation treatment should be alkaline in character, and might consist ideally of the envelope treatment with sodium hypochlorite solution.

Summary

Serious weaknesses of the official treatment of phosphorus burns are pointed out.

A rational first-aid treatment is described which can be issued in a simple portable form suitable for inclusion as standard equipment for use in the field.

Continuation treatment in hospital is also discussed.

We acknowledge with thanks the facilities generously provided by the Crookes Laboratories, which have made this investigation possible.

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THE RELATIVE NEEDS OF YOUNG MALE AND FEMALE RATS FOR VITAMIN A

BY

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It has been shown (Coward *et al.*, 1931) that if young rats were given a diet deficient in vitamin A until their reserves of that factor had been exhausted, and were then given relatively small doses of vitamin A, the response of the male rats (increase in weight in five weeks) was less than that of the female rats. When the dose of vitamin A given was rather larger the responses of the two sexes were equal, and when larger still the response of the male rats was greater than that of the female rats. This was depicted graphically by drawing the curves of response of male and female rats respectively to five graded doses of cod-liver oil, the average increase in weight of each group of rats being plotted against the logarithm to base 10 of the dose of oil given. The curve of response of the male rats was steeper than that of the female rats, and the two lines crossed at the point where the increase in weight was 13.7 gm. and the daily dose of the sample of cod-liver oil given was about 1.2 mg. (equal to about 1.8 international units of vitamin A, as determined later). The smaller response of the male rats to low doses of vitamin A indicated that the male rat was more sensitive to a shortage of this factor than was the female rat.

All the tests of low doses of vitamin A which had up to that time been carried out in our laboratory were then examined for the number of male and female rats that had died in each group, every member of any one group having received the same dose of cod-liver oil. It was found that, in 23 groups, 57 out of 288 male rats and 37 out of 277 female rats had died. Dr. J. H. Gaddum supplied a calculation based on the numbers of groups in which more males than females and more females than males, respectively, had died. The numbers were 17 and 5, and 1 in which the mortalities of male and female rats were equal. His value of χ^2 was 6.26. The table of χ^2 shows that the probability of this value of χ^2 being due to chance is between 1/50 and 1/100 (Fisher and Yates, 1938). Hence it was concluded that there was a strong probability that young male rats are more sensitive to a shortage of vitamin A than young female rats.

Since the publication of that paper many more determinations of vitamin A have been carried out in this laboratory by the same method, and it seemed worth while to examine some of our recent work to obtain more information on this point. It happened that we had used a particular sample of cod-liver oil as a standard of reference for determining the vitamin A (carotene) content of a large number of fruits and vegetables, and the international standard of reference (carotene) for determining the vitamin A content of a large number of substances containing vitamin A of animal origin. Thus it was possible not only to obtain the further information required on the relative needs of male and female rats for vitamin A but also, by separating the groups given vitamin A of animal origin from those given vitamin A (β -carotene) of vegetable origin, to see whether this difference in response between male and female rats applied to both sources of the vitamin.

Calculations of tests which fell naturally into four groups have been made. They are summarized in Table I and also put out separately, for several results all supporting the same conclusion are often more convincing than one total result.

M. Josephi, J. Mehlman, and D. Hager (*J. Pediat.*, 1941, **19**, 823) record a case of influenzal meningitis in a male infant aged 7 months who made an uncomplicated recovery after treatment with large doses of sulphapyridine and a minimal amount of serum. Culture of the spinal fluid showed *B. influenzae*.