keep on presenting new difficulties for solution. But withal he must avoid the confusion of detail and not be ashamed to rely on the simple practice of good surgery.

I am very grateful to many medical officers serving on units and in hospitals and in administrative posts, to nursing sisters, and to orderlies. They have shown that the handicaps imposed by an over-sea campaign, the necessary improvisations, and long distances are no real bar to a high standard of burns treatment when faced with intelligent enthusiasm and understanding. For such views as are not in accordance with the current teaching on burns, or appear unduly dogmatic or provocative, I am solely responsible.

FIRST-AID TREATMENT OF PHOSPHORUS BURNS

BY

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AND

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The facility with which copper combines with active phosphorus to form copper phosphide has been the basis of most methods of first-aid treatment of persons contaminated with phosphorus. The standard treatment suggests that the burning phosphorus should be extinguished with water, keeping the burned area damp and removing the patient to hospital for surgical attention as quickly as possible. The burn is treated with aqueous solutions of sodium bicarbonate and copper sulphate.

The principal objections to this treatment are that such solutions are cumbersome to carry and are not likely to be immediately available in civil defence and active service conditions, although speedy application is, of course, all-important. Also, the number of persons contaminated may be so large that immediate active surgical attention to all is not possible, and in the meantime it is necessary to repeat the application of the solution—not the best treatment for an already shocked patient. There is, further, the danger that repeated applications of fluid may wash particles of phosphorus to the periphery, with the risk of peripheral burns.

The possibility of damage to this institution by phosphorus-containing incendiaries during air attacks and the prospect of having to deal with a number of casualties among our population led us to investigate this matter with a view to producing a substance which fulfilled the following requirements: (a) it should be readily available in a compact form; (b) all the remedies should be contained in one compound; (c) it should immediately extinguish the phosphorus and inactivate the products of phosphorus combustion—i.e., phosphorus pentoxide and phosphoric acids; (d) it should be viscous and stick to the skin so as to remain in position, and also hold the particles of phosphorus *in situ*; and (e) it should be easily removed by warm water.

Godding and Notton (1942) suggested the use of copper sulphate, glycerin, and starch. Tomski (1943) recommended for trial two creams, the first containing 20% of sodium bicarbonate, and the second copper both as oleate and as sulphate. Tomski suggested that the two creams could be carried by fire guards, wardens, etc. Goldblatt and Oakeshott (1943) considered that aqueous solutions of copper sulphate would be unlikely to interact with solid phosphorus or with phosphorus dissolved in some solvent not miscible with water to produce total inactivation of the phosphorus. They suggested the use of copper oleate, with which they combined a rubber solvent.

One of us suggested the use of *sapo mollis B.P. Add. III* as the base for incorporating copper sulphate, and after many trials a compound was prepared with a final content of 4% copper salts. The damage to tissue by burning phosphorus is thought to be due not only to the heat of combustion and to the corrosive action of phosphoric acids formed as the terminal result of such combustion but also to the intensely hygroscopic action of phosphorus pentoxide, which is the intermediate stage of the change. Phosphorus pentoxide "mops up" water with great avidity and with the production of intense heat, and we

suggest that, applied to the skin, a film of water sufficient to extinguish the phosphorus flame will not be adequate to provide the pentoxide with enough water to supply its needs; thus tissue fluid is called on, causing further damage. For this reason a high proportion of water was mixed with the compound. It was also felt that water loosely held in depth over the area by such a compound might act as a better conductor of heat than air and that in this way the heat generated by the change— $P_2O_5 + 3H_2O \rightarrow 2H_3PO_4$ —would be more easily removed from the site of the injury. The method of production of the copper-soap compound is described later.

Bench and personal trials showed that the compound was extremely quick in action. Burning phosphorus was extinguished immediately and phosphide formation was very rapid. It also appeared to us that the inactivating layer of copper phosphide on the surface of a piece of phosphorus was of greater depth than with the copper sulphate solution. The black phosphide particles were very clearly visible in the green mass of the compound, giving an excellent colour contrast, and this may be important where manual removal in the operating theatre afterwards is necessary. The compound is adhesive and remains *in situ*, but is easily washed away with warm water.

Through the co-operation of the Ministries concerned, arrangements were made for tests to be carried out on experimental burns, and we are deeply indebted to Prof. G. R. Cameron and Mr. F. Burgess for their reports and for permission to publish them.

REPORT I

Treatment of Experimental Phosphorus Burns with Copper Sulphate Soap (Prof. G. R. Cameron and F. Burgess)

Adult rabbits (2 kg. body weight) were given standard phosphorus burns on the shaved skin of their backs. Under nembutal anaesthesia, 0.1 c.cm. of a 50% solution of yellow phosphorus in carbon bisulphide was applied to an area of skin enclosed by a metal ring 19 mm. in diameter, ignited, and allowed to burn for 15 seconds. Such burns are remarkably similar in depth and reaction, and heal in about 5 to 6 weeks when treated simply by water application. Two such burns were made on each rabbit—one being treated at once by repeated application of the copper sulphate ointment, which was renewed until it failed to turn brown or black, the other burn serving as a control and treated in some instances with water alone, some with the standard sodium bicarbonate-copper sulphate solution method (*Medical Manual of Chemical Warfare*, 1943, p. 50). In a third group the copper sulphate ointment was compared with copper sulphate ointment followed after two hours by 2% solution of sodium bicarbonate. In all instances the ointment was allowed to remain on the burn for several days. Comparison of healing times, judged by separation of the scabs which invariably form on the burnt surface, was adopted as the measure of effectiveness of treatment. Results are shown in Table I. It is apparent that the ointment-treated phosphorus burns heal more rapidly than burns treated with water or with the standard sodium bicarbonate-copper sulphate solutions. In the latter case there was as much as a fortnight's difference in healing times; in the former, nine days. These results are statistically significant.

With the third group of experiments, in which application of copper sulphate ointment was contrasted with ointment application followed after two hours by removal of ointment with sodium bicarbonate solution, the procedure was changed. All animals were killed on the 28th day, when healing was nearing completion, and the burns examined microscopically. The notes in Table I bring the main findings into contrast. There is no doubt that the follow-up of copper sulphate ointment application by washing with 2% sodium bicarbonate solution has aided healing; the bicarbonate solution is also excellent in removing the ointment if cleaning up of the burnt area is desired.

One striking effect of the ointment is the marked tissue reaction seen during the first 24 hours around phosphorus burns so treated. We examined microscopically the burns of five rabbits at this stage and found a great deal more oedema and cell infiltration than in burns treated by other methods. It is possible that an excessive reaction might have its disadvantages; it might lead, for instance, to more pain if the oedema were

confined under tension, or it might predispose to secondary infection. But it has not led to interference with healing; on the contrary, the ointment-treated burns have healed more rapidly than those with other treatments, accompanied though they are with less initial reaction. Perhaps the ointment has

TABLE I.—Healing of Phosphorus Burns with Various Treatments

Rabbit	Healing Times in Days	
	Copper Sulphate Ointment Treatment	Water Treatment
810	22	19
811	20	20
812	19	20
813	20	20
1594	26	55
1595	27	56
1596	34	42
1597	26	40
1628	27	31
Mean ..	24.6	33.7

Rabbit	Healing Times in Days	
	Copper Sulphate Ointment Treatment	2% Sodium Bicarbonate + 1% CuSO ₄ Treatment
1654	31	31
1655	24	45
1656	24	45
1657	33	47
1658	31	45
Mean ..	28.6	42.6

Rabbit	Healing Times in Days	
	Copper Sulphate Ointment Treatment	Copper Sulphate Ointment followed after 2 Hours by 2% Sod. Bic.
1837	Very large epidermal defect, large scab, little dermis reaction	Moderate epidermal defect, small scab, little dermis reaction
1838	Large epidermal defect, large scab, little reaction	Completely healed over
1839	Almost complete healing, very little dermis reaction	Complete healing, but epidermis thin, little reaction
1840	Moderate epidermal defect with scabbing, little dermis reaction	Healing nearly complete
1841	Scab attached to two small epidermal gaps, little dermis reaction	Scab attached to one small epidermal gap, little dermis reaction

evoked a useful counter-irritation effect; but this is purely conjecture.

We conclude from these experiments that copper sulphate ointment, in addition to being an excellent first-aid measure for phosphorus burns, is of value in the healing stages also, since it has reduced the healing time of burns in striking fashion. We would suggest that it be combined, in subsequent treatment, with sodium bicarbonate solution; for the latter allows of the easy removal of the ointment if the burn is to be inspected, assists in the disposal of any phosphorus which may still persist after ointment treatment, and tends to reduce the healing time of the burns.

Trials of preparations of this type involving emergency methods are extremely difficult to arrange. We are, however, informed by Surg. Capt. Fairley that at the time of the trials of the compound a scientist sustained a badly mangled hand due to a phosphorus grenade exploding in his hand. There was very serious tissue laceration of one hand and the loss of several phalanges of both hands. Burning phosphorus was embedded in the lacerated tissues of one hand. The compound gave excellent results, and after the patient's removal to hospital for urgent surgical treatment the soapy character of the first-aid application allowed his various injuries to be quickly cleaned up before operative treatment was undertaken. The surgeons made favourable comment on this.

The compound was issued in this hospital in wide-neck glass jars each holding half a pound. The mouths of the jars are 3 in. in diameter, thus enabling the operator to insert his fingers and obtain a sufficient quantity at once.

A sample of a German paste preparation suggested by H. Stadlinger (1944) was prepared and forwarded for examination. A comparison of this German paste and the copper-soap compound was made, and was reported on as follows.

REPORT II

Treatment of Experimental Phosphorus Burns with a German Paste (Prof. G. R. Cameron and F. Burgess)

This paste (Stadlinger, 1944) contains CuSO₄ 2 parts, bolus alba (i.e., kaolin) 70 parts, and water 100 parts. The following tests were carried out in order to compare Stadlinger's paste with the CuSO₄ ointment of McCartan and Fecitt as well as with water treatment. Groups of 10 rabbits were used. Under nembutal anaesthesia 0.1 c.cm. of a 50% solution of yellow phosphorus in carbon bisulphide was applied to an area of rabbits' skin enclosed by a metal ring 19 mm. in diameter, ignited, and allowed to burn for 15 seconds. Two such burns were made on each rabbit, one being treated at once by repeated application of the British CuSO₄ ointment, the other being treated with Stadlinger's paste, applied repeatedly until

TABLE II.—Healing of Phosphorus Burns After Various Treatments

Rabbit	Healing Times in Days	
	British Copper Sulphate Ointment Treatment	Stadlinger Paste
4231	23	32
4232	23	32
4233	23	42
4234	32	45
4235	35	45
4241	23	37
4242	23	37
4243	24	37
4244	24	38
4245	28	38
Mean ..	25.8	38.3

Rabbit	Healing Times in Days	
	Water Treatment	Stadlinger Paste
4226	42	27
4227	34	27
4228	37	42
4229	38	45
4230	50	45
4236	50	34
4237	42	37
4238	44	37
4239	44	37
4240	44	41
Mean ..	42.5	37.2

discoloration of it ceased. In another series of rabbits the Stadlinger paste method was compared with water treatment. Comparison of healing times, judged by separation of scabs which form on the burnt surface, was adopted as a measure of effectiveness of treatment. Results are shown in Table II. In addition, microscopical comparison of burns variously treated, and examined after 24 hours, was carried out to determine initial reactions to the treatment.

The mean healing time for burns treated with the British CuSO₄ ointment was 25.8 days, for the Stadlinger paste 38.3 days. The difference is significant. In the second group of rabbits the mean healing time for burns treated with water alone was 42.5 days, for the Stadlinger paste 37.2 days. This difference is barely significant. The cheering result of the investigation seems to be that the British CuSO₄ ointment is much better than the Stadlinger paste in promoting healing, while the latter has little advantage over water treatment. Microscopical examination of burns 24 hours after treatment showed somewhat more inflammation with the Stadlinger paste than with the British CuSO₄ ointment. The CuSO₄ ointment is very much easier to apply and remove than the Stadlinger paste. Secondary infection was not seen in any of these experiments.

We conclude that the British CuSO₄ ointment is much superior to the German paste.

Preparation

For convenience in handling the compound was made in $\frac{1}{2}$ -lb. lots. A 25% solution of copper sulphate in water was prepared and the requisite amount of this to give a final content of 4% copper salt was heated in a boiling-flask. Sapo mollis was heated in a water bath, and the copper sulphate solution was added hot by constant trituration on a slab. Copper precipitates as oleate, and this is thoroughly incorporated into the base between each addition. It is advisable to add the copper

sulphate solution in small successive portions. The resulting compound is a tacky homogeneous mass, and samples have kept very well for at least twelve months. The pH of the final compound, determined electrically, is 8.65 at 19° C. and 8.24 at body temperature.

Sapo mollis *B.P. Add. III* is described as the sodium or potassium soap of a suitable vegetable oil or oils or the fatty acids therefrom, other than coconut oil, palm-kernel oil, or their fatty acids. The sapo mollis used in the above preparation was supplied by British Drug Houses Ltd., and has proved very consistent and suitable for the purpose.

British Drug Houses Ltd. sent us an analysis of the sapo mollis as follows: 51.7% of fatty acids, as compared with the *B.P.* recommendation of not less than 44%. The fatty acids have a solidifying point of 17° C. (*B.P.* not higher than 31° C.), an acid value of 191.5 (*B.P.* not greater than 205), and an iodine value of 146.5 (*B.P.* not less than 83). Resin acids are absent. The soap contains no free alkali hydroxide and no free fatty acids. The total free alkali, calculated as Na_2CO_3 in 10 grammes, is equivalent to 0.2 c.cm. N/1 sulphuric acid, as against the *B.P.* limit of 1 c.cm. N/1 acid.

Conclusions

The copper-soap compound is an effective first-aid treatment of phosphorus burns.

Being a viscous and compact substance, it can be carried about easily by nurses, fire guards, etc.

In experiments, using the copper-soap compound, the healing time of wounds was substantially reduced as compared with the standard treatment.

We express our thanks to Prof. Sir Francis Fraser, Director-General of the Emergency Medical Services, and to Mr. J. B. Hunter, F.R.C.S., Sector Hospital Officer, for their great interest and help. We gratefully acknowledge the work of Prof. G. R. Cameron, Mr. F. Burgess, and Lieut.-Col. Collumbine, who carried out experiments; and also the arrangements made by Surg. Capt. A. Fairley. We are much indebted to the Medical Research Council for the help given us through Dr. F. H. K. Green and members of the Burns Subcommittee. We also wish to record our appreciation of the helpful advice and criticism given by Mr. R. F. Nunn, B.Sc., biochemist to this hospital.

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GLOBIN INSULIN: CLINICAL TRIAL

BY

J. M. MALINS, M.B., M.R.C.P.

In the present trial globin insulin (G.I.) has been used in single daily doses in 36 cases, of which 33 had had no previous treatment. All the patients gave a history of acute onset of diabetes with thirst and wasting. The diet was approximately the same for all; it contained 180 g. of free carbohydrate with an average proportion of protein and fat, and allowed patients to use the normal resources of the home kitchen or works canteen. The carbohydrate was spaced as follows: breakfast, 50 g.; dinner, 50 g.; tea, 30 g.; supper, 50 g. The range of insulin dosage was 10 to 40 units, with an average of 24, the injection being given half an hour before breakfast.

Results.—(a) In 10 cases perfect control, both clinical and biochemical, was obtained. The health remained normal, the blood sugar did not rise above 180 mg. per 100 c.cm., and the urine contained not more than a trace of sugar. The average dose of G.I. in this group was 20 units. It is notable that seven of these ten patients were regarded as exceptionally co-operative. (b) In 16 cases control was only fair. Hyperglycaemia and glycosuria persisted, although the weight and general health were on the whole maintained. The main difficulty in this group was the frequent occurrence of insulin reactions, even when the dose of insulin was increased only to control the symptoms while hyperglycaemia persisted. Six of these cases have been changed to a P.Z.I.-S.I. mixture with satisfactory results. (c) In 10 cases the control was certainly inadequate and diabetic symptoms persisted—e.g., pruritus, weakness, or occasional thirst. Five of these have been changed to a

P.Z.I.-S.I. mixture, and the others will almost certainly be treated likewise in the near future.

Hypoglycaemia.—Eighteen patients complained of insulin reactions, the symptoms in general being those common with S.I.—sweating, trembling, weakness, and hunger, relieved at once by food. In 12 cases the symptoms occurred between 11 a.m. and noon (four to five hours after the injection). In three cases the symptoms began at 6 p.m. and headache and weakness were outstanding, while relief from food was not immediate—features which resemble the P.Z.I. reaction. In one case the incidence was at 4 p.m., in the other at 8 p.m., and one man stated that he felt identical symptoms twice in one day—at 11.30 a.m. and 6 p.m.—which must be a rare event with any type of insulin. Local reactions occurred in two cases only, and were transient.

Blood-sugar Readings.—In 11 in-patients the blood sugar was studied throughout 24 hours at approximately two-hourly intervals. The diet was that described above and the average dose of G.I. was 24 units. The results were inconstant, but three average curves are shown (Figs. 1–3) which suggest that

FIG. 1.—Blood-sugar readings with 16 units of G.I.

FIG. 2.—Blood-sugar readings, 32 units G.I.

FIG. 3.—Blood-sugar readings, 40 units G.I.

with increase of dosage of G.I. the insulin activity is delayed in onset and prolonged. (1) With 16 units hyperglycaemia occurred after breakfast, but not after the midday or evening meals, while the fasting blood sugar was well above normal the next morning. In this particular case good health was maintained for six months on this regime. (2) With 32 units there was still hyperglycaemia after breakfast, but later in the day (15 hours after the injection) the blood sugar fell to dangerous levels, while the fasting sugar next morning was not grossly raised. (3) With 40 units hyperglycaemia occurred after breakfast and the midday meal, the insulin action being delayed, with very low figures throughout the early hours of the following morning (lowest figure 24 hours after injection).

Discussion

The action of G.I. has been compared with that of other insulins under experimental conditions by Bauman (1939) and Duncan and Barnes (1941), and in both papers was found to be intermediate between P.Z.I. and S.I., with maximum hypoglycaemic effect eight hours after the injection. In clinical use it has been commended by Bauman (1939, 1940) and Andrews and Groat (1940), who were able to control mild and moderately