

# THE TREATMENT OF "SHOCK" WITH SODIUM SALT SOLUTIONS

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Rosenthal (1942-5) has stated that the administration of large quantities of sodium salt solutions reduces the mortality in mice suffering from shock caused by thermal burns, trauma, and haemorrhage. Fox (quoted by Rosenthal, 1943) in man, Allen (1943) using dogs, and Prinzmetal *et al.* (1943) in mice, have also reported good results from the use of sodium chloride solutions for the treatment of shock due to thermal burns, while Cullumbine and Box (1946) have found that large quantities of sodium chloride or sodium lactate solution reduce the mortality from lewisite shock, but that different species are not equally responsive. These results have now been confirmed in mice suffering from shock caused by thermal burning and extended to rats, rabbits, and goats burnt with liquid mustard gas.

## THERMAL BURNING

Mice, weighing 18-20 g. and under nembutal anaesthesia, were used and their hind limbs immersed for 30 sec. in water which was maintained at a temperature of 80° C. Therapies were given at various time intervals after the immersion. The time of death after immersion for each mouse was carefully noted. Death occurred rapidly (2-4 hours) in 100 per cent of

untreated mice and an effort was made to find therapies which would significantly prolong the median survival time. The results were analysed by means of Fisher's method of analysis of variance for Latin squares.

*Therapy with sodium chloride.*—Table I details the results and conclusions of a typical experiment. Further experiments showed that therapies administered 30 to 60 min. after burning produced better survival times than therapies administered immediately or 120 min. after burning. In general, 0.45 per cent (w/v) NaCl solution was better than a 0.9 per cent solution which, in turn, was better than a 1.8 per cent solution. All these salt solutions were better than water. Similar results were obtained whether the sodium chloride solution was given by mouth or by intraperitoneal injection.

From the results of the above experiments, it was concluded that, of the therapies tried, 1 ml. doses of the sodium chloride solutions administered 30 min. after burning gave the best chance of survival. Therefore these therapies were assessed in less severely burned mice and the percentage mortalities of the treated and untreated groups compared.

The hind limbs of mice, under nembutal anaesthesia, were immersed for 30 sec. in water maintained at 70° C. Sodium chloride solutions were administered

TABLE I

EFFECT OF INTRAPERITONEAL INJECTION OF DIFFERENT CONCENTRATIONS OF SODIUM CHLORIDE IN AQUEOUS SOLUTION ON THE SURVIVAL TIME OF MICE SUFFERING FROM THERMAL BURNS

Therapy given 30 min. after burning	Median survival time in hours (5 mice per group)	Conclusions
1 ml. water .. .. .	10.0	(1) In general 1 ml. dosages are better than 2 ml. dosages in prolonging survival time. ( $P = 0.05$ ).
2 ml. " .. .. .	3.2	
1 ml. 1.8% NaCl .. .. .	9.9	
2 ml. 1.8% NaCl .. .. .	3.8	(2) 0.45% NaCl is better than 0.9% NaCl which in turn is better than 1.8% NaCl or water.
1 ml. 0.9% NaCl .. .. .	13.5	
2 ml. 0.9% NaCl .. .. .	9.5	
1 ml. 0.45% NaCl .. .. .	20.0	(3) All therapies but 2 ml. water and 2 ml. 1.8% NaCl produced a significant ( $P = 0.05$ ) increase in median survival time.
2 ml. 0.45% NaCl .. .. .	15.2	
Nil .. .. .	2.5	

intraperitoneally 30 min. later and the resultant total mortalities noted. These mortalities were as follows:

Untreated mice	— 24/25
1 ml. of 1.8 per cent NaCl	— 11/25
1 ml. of 0.9 per cent NaCl	— 9/25
1 ml. of 0.45 per cent NaCl	— 6/25

Hence all these therapies produced a significant reduction of the mortality, and the results agree substantially with those of Rosenthal.

*Therapy with carbohydrate and protein.*—It has been noted that, after thermal burns, the carbohydrate stores (liver and muscle) quickly become exhausted (Clark and Rossiter, 1944) and a large negative nitrogen balance soon occurs. (Cuthbertson *et al.*, 1939; Clark, Peters and Rossiter, 1945; Taylor *et al.*, 1943). Therefore the effectiveness of the early administration of aqueous solutions of glucose and of protein hydrolysate (a commercial preparation made by the enzymic digestion of casein) was assessed in experiments similar to those just described.

The therapies were: 5 and 10 g. glucose/100 ml. H<sub>2</sub>O; 2.5 and 5 g. protein hydrolysate/100 ml. H<sub>2</sub>O; the solutions were given intraperitoneally or by mouth, in 1 ml. or 2 ml. doses and at Z, Z+30, Z+60 or Z+120 min. The median survival time was not significantly prolonged by these procedures and usually it was reduced. Clark and Rossiter (1944) also found that carbohydrate feeding did not lessen the mortality among experimentally burned animals.

#### MUSTARD GAS INTOXICATION

The literature on human cases of mustard gas intoxication does not contain any clear-cut evidence as to the existence of a "shock syndrome" in this condition. Hermann (1918) has reported a condition of "shock" in some of the severe cases which he saw, but most accounts are silent on this subject. In animals (goats, dogs, rats) Cameron (1941) has described a haemoconcentration (as evidenced by increased haemoglobin and red blood cell estimations) in the first 24–48 hours after skin contamination; the changes were less marked in the rabbit. Cameron and Courtice (1942) have also described the later appearance of persistent diarrhoea and salivation leading to dehydration, loss of weight, and circulatory failure. Homer-Smith *et al.* (by communication in 1943), in a study on the toxic action of the  $\beta$ -chloroethyl vesicants in dogs, have also remarked that death is due to "anoxia" of the respiratory centres owing to peripheral circulatory failure brought on by a reduction in blood volume, which is in turn attributable to the loss of protein, electrolyte, and water through vomiting and diarrhoea, supplemented by a loss of red cells through unidentified

channels. The total circulatory plasma protein is reduced, but more water than protein is lost, so that the concentration of plasma protein rises. There is a reduction in the extra-cellular fluid, circulating plasma volume, plasma chloride, and body weight; the total circulatory red cell volume is variably reduced. As the investigators have pointed out, the

"progressive, unarrestable, and irremediable oligæmia with irreversible circulatory failure presents a close parallel to the sequence observed in dogs and man suffering fatal fire burns, haemorrhage and other forms of shock, and it is to be anticipated in men suffering severe vesication from mustard gas burns of the skin, and in whom a variable degree of systemic intoxication is superimposed on the loss of protein, the electrolytes and water through the vesicated areas."

In view of these reports of early haemoconcentration and later dehydration and electrolytic loss in mustard gas contaminated animals, it was decided to assess the value of sodium chloride administration in such animals. Three species have been studied, viz., the rat, rabbit, and goat.

*Rats.*—Rats (*ca.* 150 g.) were used first as the test animals; in all experiments they were contaminated by applying 10 mg./kg. of mustard gas in 1 per cent (w/v) alcoholic solution to the shaven area of the back. Precautions were taken to prevent the rats licking the contaminated area and ingesting the contaminant. The results are given in Table II.

We can conclude that in mustard gas contaminated rats:

(i) Sodium chloride solutions are an effective treatment and the sooner they are administered the better.

(ii) Although the difference is not statistically significant, sodium chloride is probably more effective when given by mouth than when given intraperitoneally.

(iii) Sodium lactate is ineffective either by mouth or intraperitoneally. (This is contrary to our experience in the treatment of lewisite intoxicated animals, and to Rosenthal's results with severely burnt mice. It emphasizes the possibility that different biochemical reactions may be involved.)

(iv) Water produced no significant effect, which suggests that electrolyte loss is a more important factor than mere dehydration in the pathology of mustard gas poisoning.

*Rabbits.*—Rabbits were contaminated with 150 mg./kg. of mustard gas (pure) on the shaven area of the back; licking of the area was prevented. Half the rabbits were treated with 150 ml. (given in two doses

TABLE II  
EFFECT OF SODIUM SALT SOLUTIONS ON THE SURVIVAL OF RATS INTOXICATED WITH MUSTARD GAS

Treatment	Time of administration after contamination	Route	No. of animals	No. of deaths in 21 days	Per cent mortality
Nil	—	—	70	56	80
15 ml. 0.9% NaCl	At once	I.P.	20	6	30
15 ml. 0.9% NaCl	15 minutes	I.P.	20	5	25
15 ml. 0.9% NaCl	30 "	I.P.	20	12	60
15 ml. isotonic sodium lactate	15 "	I.P.	10	9	90
15 ml. water	15 "	Oral	10	7	70
15 ml. 0.9% NaCl	15 "	"	20	6	30
1 ml. 15% NaCl	15 "	"	10	2	20
1 ml. 30% NaCl	15 "	"	10	2	20
15 ml. isotonic sodium lactate	15 "	"	10	8	80

(I.P. = intraperitoneal)

This table shows the mortality rate in untreated rats to be 80 per cent and in rats treated with sodium chloride 37 per cent (significant at  $P = 0.000,000,1$ ).

of 75 ml. at 2 and 4 hours after contamination) of 0.9 per cent NaCl by mouth; the other half were not treated. The 28-day mortalities were:

Treated rabbits — 2/10—i.e., 20 per cent.  
Untreated rabbits — 7/10—i.e., 70 per cent.

This reduction in mortality is significant at  $P=0.04$ , if we take into account that the difference is in the right direction. The incidence and severity of diarrhoea and salivation and the loss of weight were much less in the treated than in the untreated group.

**Goats.**—The shaven backs of goats (circa 30 kg.) were contaminated with 35 mg./kg. mustard gas. The 0.9 per cent NaCl solution was given subcutaneously or by mouth, 1 litre at 2 hours and 1 litre at 4 hours after contamination. The 28-day mortalities for the goats in the various groups were: 7/10 in untreated goats, 7/10 in goats receiving NaCl subcutaneously, and 6/10 in goats given the NaCl by mouth. Hence the administration of sodium chloride did not reduce the mortality from mustard gas contamination in goats. Given subcutaneously, the saline solution caused massive pulmonary oedema in some of the goats (4/10), whereas by mouth it led to an increased incidence of diarrhoea (5/10, cf. 2/10 in the untreated group).

Therefore, the order of efficacy of sodium chloride solutions in the treatment of the oligæmia of mustard gas intoxication in the three species tested descends as follows: rats, rabbits, and goats. This is also, in our experience, the descending order of the ability of the different species to tolerate large quantities of sodium chloride solution.

#### SUMMARY

In confirmation of previous workers, it has been found that sodium chloride solutions increase the

survival time and reduce the mortality rate of mice suffering from shock induced by immersion in hot water. The best results were obtained by giving 1 ml./0.45 per cent (w/v) sodium chloride solution 30 min. after burning mice weighing about 20 g. Glucose and protein hydrolysate solutions did not increase the survival time in our experiments.

These results suggested the use of sodium salt solutions in the treatment of mustard gas intoxication. This form of therapy was highly effective in rats and rabbits; it was ineffective in goats.

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