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GAS GANGRENE OF THE HIGH VELOCITY MISSILE WOUND

II: An experimental study of penicillin prophylaxis

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Introduction

THIS further experimental series was carried out to determine whether prophylactic systemic penicillin given after a high velocity missile wound affected the onset of gas gangrene (clostridial myonecrosis) in the sheep leg wound preparation used previously (Thoresby and Watts 1967, Thoresby and Matheson, 1967).

The literature concerning the clinical value of early penicillin therapy is conflicting; though it forms part of the standard treatment regime (Field Surgery Pocket Book 1962).

Jeffrey and Thompson (1944) enthusiastically recommended parenteral penicillin, as did Fisher et al (1944), such views being supported by the series of guinea pigs experimentally infected by Altmeier et al (1947). But North (1947), who added penicillin to his treatment regime late in his series, doubted its value. This latter conclusion was endorsed by Cutler and Sandusky (1945) Stammers (1945), Patterson et al (1945) and Conway (1946).

The experimental guinea pig series of Altmeier et al (1947) is not directly comparable to the clinical situation, because the penicillin was injected in one leg simultaneously with the clostridial contamination of the freshly incised wound of the other leg. The closer simulation of the high velocity missile wound in man provided by the sheep leg preparation of Hopkinson and Watts (1963) has previously been described (Thoresby and Watts 1967). Surface wound inoculation (Altmeier et al 1947) is not the normal mechanism of primary bacterial contamination in high velocity missile injuries. Contamination results from the sucking effect of the partial vacuum arising in the temporary cavity which draws in contaminating particles from both entry and exit wound surfaces (Dziemian and Herget 1950, Thoresby and Darlow 1967). The literature on *cavitation* has recently been reviewed (Thoresby 1966).

In the present series parenteral penicillin was given 3/4 hours after wounding as a conservative approximation of the interval that might elapse in the field. Only one other dose of penicillin was administered after a further 6 hours (normally in the field, primary surgical facilities would be available by this time). This allowed the prophylactic role of early penicillin to be evaluated, rather than any effect that prolonged therapy might have had on established gas gangrene (myonecrosis).

Materials and Methods

Wound: This was the 0.22 in (5.6 mm) 'Hornet' high velocity bullet wound preparation of the sheep's hind leg developed by Hopkinson and Watts (1963).

Contamination: *Cl. oedematiens* (5×10^6 spores/1 ml) was used as described previously by Thoresby and Watts (1967), the culture suspension being spread over 4 square inches of battledress khaki cloth. This clothing simulant was fixed over the wound entrance surface (Thoresby and Darlow 1967), the spores being sucked into the wound by the cavitation process (Thoresby 1966).

Anaesthesia was chloroform by inhalation following premedication with 2 ml (1.2 mgms) I.M. injection of atropine given half an hour previously. The same anaesthetic technique was used for wounding and for surgical treatment six hours later.

Procedure: Twelve experiments were performed. In each experiment a group of three sheep (adult ewes) matched for size, weight and breed were used. One of the three animals had the wound treated by incision at 6 hours, this and one untreated animal having been given parenteral penicillin at 3/4 hours and again 6 hours later. The third (the control) animal had no treatment after wounding.

Penicillin: The standard recommended adult doses of 300,000 units of benzylpenicillin and 600,000 units of procaine penicillin (Field Surgery Pocket Book 1962) were used, being given by deep intramuscular injection into the undamaged hind leg.

Operation: The operative procedure of incision involved laying open the bullet track as described previously (Thoresby and Matheson, 1967).

Autopsy was carried out on every animal, either as soon as practicable after death or when sacrificed after 200 hours survival. Clostridial myonecrosis seen at autopsy was

confirmed histologically and by recovery of the contaminating clostridial organisms as previously described by Thoresby and Watts (1967) and Thoresby and Matheson (1967).

Results

The results are shown in Table I from which animals not having a muscle wound were excluded from Table I (sheep 3A and 4A had skin wounds only).

Controls (no treatment—Animal A in each group)

All the control sheep died with typical gas gangrene (myonecrosis) of the wound, within 20-65 hours, save one (6A) which survived to 90 hours.

Penicillin alone (Animal B in each group)

Of the 12 sheep 10 survived and had normal healing wounds when sacrificed at 200 hours. Two (8B, 9B) died of typical gas gangrene (myonecrosis) at 60 hours.

Penicillin and wound incision (Animal C in each group)

Only one animal (2C) survived, its wound was healing well when sacrificed and clostridia were not recovered. The remaining sheep died of gas gangrene within 20-65 hours.

Discussion

With one exception (6A) all animals that developed gas gangrene died within 20-65 hours of wounding irrespective of the treatment given. This result resembled that found in an earlier series (Thoresby & Watts 1967) of untreated animals infected with *cl. oedematiens*. The gas gangrene deaths in the present series included two animals (8B & 9B) treated with penicillin. This contrasts with the two animals in the previous series of Thoresby and Matheson (1967) which were treated by wound excision alone: though eventually dying of gas gangrene these animals survived twice as long as the controls in their group. These findings suggest that though prophylactic penicillin will often prevent the onset of gas gangrene, should myonecrosis, however, occur, then penicillin has no effect on the course of the disease. This may explain the failure of penicillin therapy reported in some of the series of gas gangrenous war wounds.

Simple wound incision nullified, save in one animal (2C), any benefit that might have been expected from penicillin prophylaxis. It is probable that, as the blood supply of most muscles enters predominantly from one or both ends (Campbell and Pennefather 1919, Le Gros Clark & Blomfield 1945), a transverse incision joining the exit and entrance of the through-and-through muscle wound is likely to increase the local area of ischaemia surrounding the missile track. This would encourage the germination of clostridia by reducing the oxidation/reduction potential (Eh) (Fildes 1927, 1929a, b) and concurrently reduce the local tissue concentration of diffused penicillin.

Conclusions

Under the experimental conditions prophylactic penicillin at 3/4 hours and 6 hours alone, in ten out of twelve standard deliberately contaminated sheep bullet wounds prevented the onset of gas gangrene: in two animals where this failed, no prolongation of survival occurred compared with control animals. Penicillin protection was prejudiced when simple transverse wound incision was carried out.

These observations seem to confirm experience in human clinical practice, namely that early penicillin administration is likely to be of benefit in the prevention of gas

gangrene, particularly in small perforating wounds comparable to those inflicted in the present experimental series. As it is known that the area of ischaemia if untreated around the wound track increases steadily during the first six hours after wounding (Hopkinson and Watts 1963), the much larger initial doses given by Altemeier et al (1947) might be used with advantage in the field, rather than those used in this series which were based on the recommendations in the Field Surgery Pocket Book (1962).

The present and previous (Thoresby and Matheson, 1967) series give experimental support to the doctrine that early and adequate excision is the mainstay of any treatment regime designed to prevent the development of gas gangrene in a high velocity missile wound of muscle. To such treatment prophylactic penicillin is likely to be a beneficial adjuvant, particularly in the case of small perforating wounds.

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Table I
Survival Time (hours) after Wounding

GROUP	A CONTROL		B PENICILLIN ALONE		C PENICILLIN + INCISION	
	Weight Kg	Hours	Weight Kg	Hours	Weight Kg	Hours
1	76	40*	79	200	79	20*
2	89	40*	83	200	79	200
3	94	—	87	200	85	50*
4	57	—	85	200	78	65*
5	76	40*	79	200	83	35*
6	76	90*	79	200	92	60*
7	68	65*	56	200	46	45*
8	59	60*	44	60*	45	25*
9	46	65*	59	60*	52	60*
10	92	40*	75	200	75	60*
11	52	65*	57	200	57	50*
12	49	60*	63	200	59	55*

*Death from gas gangrene.

The excess survival in B ('Penicillin alone') is significant.