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TREATMENT OF SEVERE THERMAL BURNS WITH DIGOXIN AND INTRAVENOUS FLUIDS

by

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with the assistance of

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INTRODUCTION

Burn shock endangers the patient principally during the first 24 to 48 hours and is responsible for many deaths from burns (1). The cardiodynamic factors usually associated with burn shock include decreased cardiac output, peripheral vasoconstriction, decreased blood volume, and a late fall in arterial blood pressure (2) Blalock (3, 4) and others (5-10) have concluded that the principle factor in the production of burn shock in humans and animals is a reduction in venous return to the heart from loss of plasma into the burned area. Harkins (5) and Evans et al (10) have studied this fluid loss carefully, and the latter group has developed a formula for calculating the fluid required to restore blood volume.

Work at this laboratory (11) recently demonstrated that cardiac output in dogs invariably falls precipitously following burn before there is any change in blood volume, heart rate, or right atrial pressure. This observation was confirmed by Dobson and Warner (12) and by studies at the Brooke Army Medical Center (13). In addition, Hardy et al (14) measured cardiac output in humans during the first day following burn and found a low average output of 3.7 liters/minute in six subjects studied by the T 1824 dye dilution method.

Several possible theories are available to explain the fall in cardiac output in the presence of a normal blood volume. First, blood may be "trapped" and not available to the general circulation. If this is true, then expansion of the blood volume by intravenous fluids might be expected to restore cardiac output. However, Gilmore (15) reports minimal effect on the decreased cardiac output from infusions which increased plasma volume as much as 17 percent above normal and caused a rise in right atrial pressure. Peripheral vasoconstriction might lead reflexly to a decrease in cardiac output; however, a sympatholytic agent (dibenamine) did not modify this cardiac output change after burns (16).

A third possible mechanism to explain the cardiac output fall is primary myocardial injury. Several findings support this theory: (1) cardiac output falls in the presence of a normal blood volume and is not restored by an increase in volume, (2) right atrial pressure does not fall along with the cardiac output, and (3) the decrease in output is a result of a decrease in stroke volume. If direct myocardial injury does occur, a beneficial effect might be obtained by treatment with drugs which increase the force of myocardial contraction. To test this possi-
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A third possible mechanism to explain the cardiac output fall to primary myocardial injury. Several findings support this theory: (1) cardiac output falls in the presence of a normal blood volume and is not restored by an increase in volume; (2) right atrial pressure does not fall along with the cardiac output, and (3) the decrease in output is a result of a decrease in stroke volume. If direct myocardial injury does occur, a beneficial effect can also be obtained by treatment with drugs which increase the force of myocardial contraction. To test this possi-
bility; burned animals were treated in the present experiments with digoxin and/or fluids, and cardiac output was measured.

MATERIALS AND METHODS

Thirty-eight mongrel dogs (mean weight = 11.3 kg; range 6.7-18.1 kg) were divided into seven groups of five or six animals each and were treated as follows: Group A - no treatment; Group B - digoxin after the one hour postburn measurement; Group C - fluids after one hour; Group D - both digoxin and fluids after one hour; Group E - fluids immediately after burn; Group F - digoxin immediately after burn; and Group G - fluids and digoxin immediately after burn.

The preparation of animals, procedures for inflicting the burn, and methods of measuring blood pressure have been described elsewhere in detail (11). Cardiac output was measured by externally monitored radioiodinated serum albumin (RISA) dilution curves (17). Plasma volume was measured by RISA dilution, utilizing an extrapolated to value (17). Dextran* was used as the fluid for blood volume expansion and was given intravenously by slow drip in quantity estimated from control studies to restore blood volume to normal. Digoxin** was given slowly intravenously in an average dose of 0.08 mg/kg.

The experimental procedure was as follows: the animals were anesthetized with 30 mg/kg pentobarbital sodium intravenously. Cardiac output, blood volume, femoral arterial pressure, and heart rate were measured and a 20 cal/cm² 10 per cent body surface burn was accomplished. The measurements were repeated at one, two, and three or four hours postburn. Digoxin was given and/or fluids begun at the times described above. Survival was not measured beyond the fourth hour.

RESULTS

Cardiac Output and Blood Volume

Each change or difference described in the results had a value for P < .03 by Student's "t" test. The small control series (Figure 1-A,

* Expandex, 6 per cent, in isotonic sodium chloride, Baxter Laboratories, Inc.

** Lanoxin, Burroughs Wellcome and Co.
Tables 1 and 2) in representative of larger studies previously reported (11). Cardiac output fell to 48 per cent of control values by one-hour postburn and continued to decline slowly, reaching 36 per cent by four hours. Blood volume decreased by 18 per cent after one hour and fell an additional 8 per cent by four hours. When treatment was withheld until after the first hour measurement (Groups B, C, and D), cardiac output had fallen to 51 per cent (not significantly different from the control).

Upon restoration of blood volume alone by administration of fluids one hour postburn (Figure 1-C), output rose to 68 per cent of control and stabilized at that level. When digoxin alone was given following the one-hour measurement (Figure 1-D), cardiac output rose to 71 per cent, or the same increase as that resulting from restoration of volume. However, output declined severely in this latter group in the two instances measured at four hours. Blood volume loss was not influenced by digoxin administration. When blood volume was restored and digoxin was also given (Figure 1-D, one hour postburn, output rose to 135 per cent of control.

When fluid treatment was begun immediately postburn (Figure 1-E) to prevent any fall in blood volume, the initial fall in cardiac output was not prevented; however, by two hours postburn, the cardiac output had risen to 78 per cent of control and was maintained at that level. Digoxin given immediately postburn (Figure 1-F) reduced the extent of the output decline, with an average value of 74 per cent of control by four hours postburn. Once again, no effect was noted on blood volume loss. When both digoxin and fluids were begun immediately postburn (Figure 1-G), cardiac output was maintained at control levels.

Blood Pressure and Heart Rate

In general blood pressure and heart rate fell slightly following burn and returned to control levels by four hours (Table 3). Treatment by any of the methods employed did not modify this pattern. Specifically, no decrease in heart rate was found in those receiving digoxin.

DISCUSSION

Either adequate fluid therapy or digitalization was partially effective in preventing the fall in cardiac output or in restoring it to control levels. In Group C blood volume restoration after one hour led
to a rise in cardiac output from 48 per cent to 68 per cent. Fluids administered immediately to prevent a decrease in blood volume (Group E) also diminished the fall in cardiac output a similar amount.

Digoxin administration alone (Groups B and F) resulted in cardiac output changes similar to those following fluid administration in spite of declining blood volume. In Group D fluid administration in association with digoxin at one hour led to a rise in cardiac output to above normal and administration of both of these agents immediately postburn (Group G) prevented the fall in cardiac output.

It has long been accepted that the primary effect of the administration of cardiac glycosides is to increase myocardial contractility (18). This action improves cardiac output of the failing heart (19), but not of the normal heart (20). The results of the present study suggest, then, that following burn there is a depression of myocardial contractility with reduction in cardiac output, and that digoxin effectively reverses this by restoring myocardial contractility to normal. It is possible that the beneficial effect of digitalization was not mediated through an improvement in cardiac contractility but by some effect on the heart rate or on the peripheral venous bed. However, the administration of digoxin in these experiments led to no change in heart rate; and recent work describes the peripheral action of digitalis to be venous pooling (21), which would tend to reduce cardiac output. Measurement of ventricular filling pressures would be useful in validating the assumption that myocardial contractility is improved.

The importance of administering adequate fluids in early treatment of burns is unquestioned. It would appear from these animal experiments that digitalization may be beneficial in the absence of fluid administration. Even when fluid therapy was adequate, however, digitalization was necessary in order to restore cardiac output to normal levels in dogs during the first few hours following burn.

The findings of Hardy et al (14) suggest that the cardiac output fall in animals may also occur in humans following severe burn. Addition of digoxin to the early therapy of burns may be useful in preventing or combating burn shock. In event of the military use of nuclear weapons, mass burn casualties might be expected and even the simplest intravenous fluids may be difficult to obtain in the field. The present experiments suggest that under these circumstances, digitalization may be beneficial until fluids are available for administration.
SUMMARY

The effect of early treatment of burn shock in dogs with fluid replacement and/or digoxin are described. Fluids or digoxin partially restore cardiac output, but both are required to restore flow to normal or to prevent its fall. These findings suggest that there is an element of myocardial failure immediately after burn, which may be effectively treated with the cardiac glycosides. This therapy is suggested (1) before fluids are available for use and (2) in addition to adequate fluid therapy.
REFERENCES


16. Gilmore, J. P. The effect of dibenamine, levarterenol, or splenectomy upon the course of burn shock in the dog. Naval Medical Field Research Laboratory, Camp Lejeune, N. C. Report NM 006 014 04. 04. 06. 7: 25, 1956.


### Table 2

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* Mean of four dogs.

1 Bracket indicates no true linear quadrature for calculation.

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559
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<td>Diluted 1% Femoral</td>
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* Number of animals tested is indicated in parentheses
* All figures in table are mean and standard error values
MEMORANDUM FOR DEFENSE TECHNICAL INFORMATION CENTER
ATTN: OCQ/MR WILLIAM BUSH

SUBJECT: DOCUMENT REVIEW

The Defense Threat Reduction Agency's Security Office has reviewed and declassified or assigned a new distribution statement:

- AFSWP-1069, AD-341090, STATEMENT A
- DASA-1151, AD-227900, STATEMENT A
- DASA-1355-1, AD-336443, STATEMENT A
- DASA-1298, AD-285252, STATEMENT A
- DASA-1290, AD-444208, STATEMENT A
- DASA-1271, AD-276892, STATEMENT A
- DASA-1279, AD-281597, STATEMENT A
- DASA-1237, AD-272653, STATEMENT A
- DASA-1246, AD-279670, STATEMENT A
- DASA-1245, AD-419911, STATEMENT A
- DASA-1242, AD-279671, STATEMENT A
- DASA-1256, AD-280809, STATEMENT A
- DASA-1221, AD-243886, STATEMENT A
- DASA-1390, AD-340311, STATEMENT A
- DASA-1283, AD-717097, STATEMENT A
- DASA-1285-5, AD-443589, STATEMENT A
- DASA-1714, AD-473132, STATEMENT A
- DASA-2214, AD-854912, STATEMENT A
- DASA-2627, AD-514934, STATEMENT A
- DASA-2651, AD-514615, STATEMENT A
- DASA-2536, AD-876697, STATEMENT A
- DASA-2722T-V3, AD-518506, STATEMENT A
- DNA-3042F, AD-525631, STATEMENT A
- DNA-28212-1, AD-522555, STATEMENT A
If you have any questions, please call me at 703-325-1034.

ARDITH JARRETT
Chief, Technical Resource Center