The Treatment of Shock Associated with Myocardial Infarction

By George C. Griffith, M.D., W. B. Wallace, M.D., Burt Cochran, Jr., M.D., W. E. Nerlich, M.D., and W. G. Frasher, M.D.

As a background to the problem of shock associated with acute myocardial infarction, a review of 816 recent consecutive and proved cases has been made. One hundred and sixty-one cases met the arbitrary criteria for the definition of shock. Therefore, shock was found to have occurred in 20 per cent of the patients with myocardial infarction. The mortality was 81 per cent (128 patients died).

In the present study, 134 patients with acute myocardial infarction in shock were treated. All of these patients were first treated by strictly routine measures, including digitalis when indicated. Sixty of the 134 patients were relieved by prompt routine therapy given within a three-hour period of time. The remaining 74 patients were treated by (1) retrograde arterial infusion, (2) the newer sympathomimetic drugs such as methoxamine, isopropylnorepinephrine and norepinephrine and (3) other agents such as cholinesterase and cortisol. An evaluation of these methods was made and the over-all mortality of shock as associated with myocardial infarction was reduced from 81 per cent to 48 per cent.

Considerable controversy exists concerning the value of various measures employed in the treatment of shock accompanying acute myocardial infarction. In spite of the high mortality rate attending this condition, antishock measures rarely have been instituted until considerable time has elapsed and hope for spontaneous recovery has been abandoned. In fact, hopelessness often has been the criterion for treatment. It is noteworthy, therefore, that results of an investigation recently completed at the Los Angeles County Hospital disclose that the promptness with which measures for combating shock are instituted is a key factor in recovery, overshadowing in importance the particular method or combination of methods used in bringing shock under control.

In this paper, evidence is presented of the importance of the time element in the successful treatment of the shock syndrome when associated with myocardial infarction. Also, results obtained with various modes of treatment at the Los Angeles County Hospital during an 18-month period in 1951 and 1952 are discussed. Statistics for a comparable 18-month period (1949–51) in which specific antishock measures were not employed afford an additional basis for evaluation of measures employed in the treatment of shock in the 1951–52 period.

Shock Defined

For the purposes of this investigation, shock is defined as a condition of marked hypotension, lasting for an hour or longer, and accompanied by signs of peripheral circulatory collapse. In a patient whose blood pressure has previously been within normal limits, a systolic blood pressure reading of 80 mm. Hg or below is accepted as evidence of shock. In the formerly hypertensive patient, a systolic blood pressure of 100 mm. Hg or below evidences shock.
Material

The Control Group. A review of the records of the Los Angeles County General Hospital discloses that during an 18-month interval in 1949–1951, 816 patients gave proof of myocardial infarction, the diagnosis having been established by incontrovertible electrocardiographic evidence or verified at necropsy. One hundred and sixty-one of the 816 evidenced shock as defined in this investigation, a shock incidence of 19.7 per cent; of these 161 cases, 128 died, a mortality incidence of 80 per cent.

The Experimental Group. The experimental group was composed of 134 patients who were treated for shock coupled with unmistakable recent myocardial infarction during the 18-month period of this investigation (1951–1952). If the percentage of shock mortality approximated that of the control period, we could assume that 107 of the 134 patients would die. Our records show that only 64 patients died; a shock mortality incidence of 47.8 per cent.

Methods of Treatment and Results

Importance of Time Element

As stated earlier, the promptness with which measures for combatting shock were instituted was of paramount importance: of the 134 patients with myocardial infarction treated for shock during the 1951–1952 interval, 60 received treatment within three hours of the onset of the shock syndrome. Of the 60, only 13 per cent died. In contrast of 74 patients who received treatment after lapse of a three-hour interval, 76 per cent died. (See table 1.)

| Table 1.—Results of Treatment Shock Associated with Myocardial Infarction |
|-------------------------------------------------|------------------|
| No. of Cases | Survived, % |
| Control Group (1949–51) | 161 | 19 |
| Test Group (1951–52) | 134 |  |
| (1) Treated within 3 hrs. | 60 | 87 |
| (2) Treated after 3 hrs. | 74 | 24 |

Routine Methods of Treatment

All 134 patients were first treated by such obvious routine measures as proper positioning, relief from pain and cold, easing of anxiety, and control of other factors which might contribute to shock. Continuous administration of oxygen to each patient through a nasal catheter or mask, or by means of intermittent positive pressure, assured a sufficient supply of oxygen at all times. Phlebotomy or administration of ethyl alcohol vapor was required in instances of persistent failure.

Morphine sulfate, administered intravenously, proved of value in relieving shock, a pressor effect occurring promptly even in comatose patients. (We feel that morphine's advantages outweigh certain undesirable features, such as the aggravation of anoxemia by respiratory depression. Nevertheless, overtreatment with morphine can be detrimental, particularly in the elderly patient.)

Patients with congestive heart failure received intravenous doses of digitalis, strophanthus or other glycosides in order to support fully the uninfarcted myocardium. In the absence of heart block, premedication with quinidine proved a worthwhile procedure.

Arrhythmias were quickly brought under control, and anticoagulants were administered routinely unless a definite contraindication existed.

Additional Treatment

If shock was not relieved by “routine” methods, additional measures were tried. Nine patients received intravenous infusions: a pressor effect was obtained in three instances, and shock was controlled in two.

Retrograde arterial infusions were given to 25 patients. A pressor effect was obtained in 19 cases; in 12 of these, shock was brought under control. A detailed analysis of results in 12 cases receiving arterial infusions will be found in table 2. Although a bulky apparatus was used in the first of the infusions, a simplified, portable apparatus similar to that described by Page has proved more suitable.1 Any available artery can be used; it has, however, been our practice to insert large-
### Table 2.—Arterial Infusion in Coronary Shock. An Analysis of 12 Cases

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Shock Hours</th>
<th>Agent cc.</th>
<th>Adjunct Pre-Post</th>
<th>Infarct</th>
<th>Relief Hours</th>
<th>Fate</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>F</td>
<td>24</td>
<td>B-500</td>
<td>ivP, B—V</td>
<td>Anteroseptal</td>
<td>3</td>
<td>Died 5½ hrs.</td>
<td>3° heart block</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>4½</td>
<td>B-300</td>
<td>iv, V—ivB, V</td>
<td>Anteroseptal</td>
<td>13</td>
<td>Died 31 hrs.</td>
<td>Embolism Perforated peptic ulcer</td>
</tr>
<tr>
<td>70</td>
<td>F</td>
<td>6</td>
<td>B-500 Lac-90</td>
<td>Routine</td>
<td>Postero septal</td>
<td>63</td>
<td>Died 65 hrs.</td>
<td>3° heart block Arrhythmia Pneumonia</td>
</tr>
<tr>
<td>77</td>
<td>M</td>
<td>6</td>
<td>B-500 d/s-900</td>
<td>ivP—ivP—</td>
<td>Postero septal</td>
<td>*</td>
<td>Died 34 hrs.</td>
<td>Arrhythmia</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>6</td>
<td>P-250</td>
<td>V—V</td>
<td>Anterior</td>
<td>*</td>
<td>*Lived</td>
<td></td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>4</td>
<td>B-500</td>
<td>Routine</td>
<td>Anterior</td>
<td>*</td>
<td>*Lived</td>
<td></td>
</tr>
<tr>
<td>71</td>
<td>F</td>
<td>3</td>
<td>d/s-1000, B-500</td>
<td>V—V</td>
<td>Antero-posterior</td>
<td>*</td>
<td>Died 13 days</td>
<td>Cardiac tamponade</td>
</tr>
<tr>
<td>58</td>
<td>M</td>
<td>20</td>
<td>P-500</td>
<td>R—RAI</td>
<td>Anterior</td>
<td>3</td>
<td>Died 4 hrs.</td>
<td>Repeat RAI to no avail</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>7</td>
<td>P-250</td>
<td>V—V, C</td>
<td>Anterior</td>
<td>3</td>
<td>Died 4 hrs.</td>
<td>Cortisone</td>
</tr>
<tr>
<td>78</td>
<td>M</td>
<td>5</td>
<td>P-250</td>
<td>V—V</td>
<td>Anterior</td>
<td>*</td>
<td>*Lived</td>
<td>Embolism</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>6</td>
<td>P-250</td>
<td>V—G, V</td>
<td>Anterior</td>
<td>*</td>
<td>*Lived</td>
<td>Cortisone</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>3</td>
<td>B-275</td>
<td>V—R</td>
<td>Anterior</td>
<td>*</td>
<td>*Lived</td>
<td></td>
</tr>
</tbody>
</table>

**Shock Hours:** Hours in shock before arterial infusion.

**Adjunct Pre—Post:** Treatment before and after arterial infusion B (whole blood), P (plasma), Lac (M/6 sodium lactate), d/s (5% glucose in normal saline), iv (intravenous), V (vasopressor drugs), R (routine coronary regimen), RAI (retrograde arterial infusion), C (Cortisone).

**Relief Hours:** Time in hours shock was relieved. * Permanent relief of shock.

**Fate:** Figures indicate time after completion of arterial infusion that the patient expired.

gauge polyethylene tubing into the radial artery just proximal to the styloid process. In considering our results (table 2), it should be noted that we have employed lower perfusion pressures than are commonly reported, and that the infusion times have been prolonged accordingly. (Perfusion pressures were generally 100 to 140 mm. Hg, but lower in a few instances; the duration of infusions was usually 20 to 70 minutes, but in a few instances longer.) Plasma or blood has been employed in most instances.

One hundred and five episodes of shock were treated with three of the newer sympathomimetic amines: norepinephrine, methoxamine, and isopropynorepinephrine. Each has proved of value, particularly with early treatment.

**Norepinephrine.** Early reports on the effects of norepinephrine suggested that an apparent tendency of the preparation to produce ventricular arrhythmias might constitute a considerable hazard in the presence of myocardial infarction. Later reports have been more encouraging. Norepinephrine has been employed without untoward effects in the treat-
ment of hypotension following thoracolumbar sympathectomy, and, more recently, has received clinical trial in the treatment of seven patients with coronary shock. Ventricular irritability did not follow. Norepinephrine was used in 30 cases; shock was controlled in 17 of these. We have been impressed with the effectiveness of norepinephrine when used early in shock, or when employed late in the treatment after other pressor amines have failed.

Administration was as follows: 1000 cc. of 5 per cent glucose in water to which two vials (8 mg.) of norepinephrine had been added were supplied by intravenous drip through a polyethylene tube introduced for a distance of six or eight inches into the antecubital vein. Drip was begun at an initial rate of 10 drops per minute—delivering 8 gamma per minute—and rate of drip was increased or slowed as necessary to maintain a systolic blood pressure of 120. Drip was continued for as long as required (even as long as 72 hours). It is important that blood pressure be taken every 15 or 20 minutes.

**Methoxamine.** Forty-nine patients received methoxamine. Pressor effect was obtained in 14 patients and shock controlled in 10 patients. No pressor effect was obtained in 35 instances: this we attribute in part to the fact that response to the drug is lost relatively early in shock. Methoxamine proved useful within the first few hours of shock, usually as an adjunct to other therapy.

Methoxamine was administered either intramuscularly (20 mg. dose) or intravenously (5 mg. dose, given slowly and repeated as needed).

**Isopropynorepinephrine.** Twenty-six patients were given isopropynorepinephrine. A pressor response was obtained in 10 patients, while shock was controlled in seven patients. No pressor effect was seen in 16 patients. This drug has proved particularly useful in cases of shock associated with complete heart block, bundle branch block or prolonged congestive failure. Although isopropynorepinephrine's action in coronary shock has not been established with definiteness, its inotropic and chronotropic cardiac effects are presumably accompanied by medullary stimulation, coronary dilation, and relief from excessive peripheral vasoconstriction.

Two or 3 mg. of isopropynorepinephrine are given slowly intravenously, followed by 7.5 or 15 mg. given under the tongue as needed after shock has been overcome (at 10 to 15, or at 30 minute intervals).

**Comparison of the Effects of Epinephrine, Norepinephrine, Isopropynorepinephrine and Methoxamine.** A comparison of the effects of these four drugs as observed by us is worthy of note. (See table 3.) In the patients in shock with an intact conduction system, epinephrine, norepinephrine and methoxamine raise the blood pressure, while isopropynorepinephrine fails to do so. The heart rate is increased by epinephrine and isopropynorepinephrine. Norepinephrine has no effect on the rate. Methoxamine slows the heart rate. Epinephrine and norepinephrine stimulate an already sensitized myocardium in the experimental animal. In our experience there has been no unusual arrhythmia noted from the use of norepinephrine in small or large doses when regulated by the pressor response. In patients in shock where there is complete auriculoven- tricular dissociation isopropynorepinephrine not only increases the ventricular rate preventing Adams-Stokes attacks but also has demonstrated a remarkable pressor effect.

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**Table 3.—A Comparison of Hemodynamic Effects of Some Sympathomimetic Amines**

<table>
<thead>
<tr>
<th>Effect On:</th>
<th>Epinephrine</th>
<th>Norepinephrine</th>
<th>Isopropynorepinephrine</th>
<th>Methoxamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic blood pressure</td>
<td>+</td>
<td>+</td>
<td>*</td>
<td>+</td>
</tr>
<tr>
<td>Normal sinus rhythm (rate)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>3° heart block (ventricular rate)</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Total peripheral resistance</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Stimulation of sensitized myocardium</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>0</td>
</tr>
</tbody>
</table>

* Normotensive adult volunteers; in shock blood pressure is raised (see text).
  + (increase), 0 (no change), − (decrease)
**Dosages.** Dosage schedule of these sympathomimetic amines must be adjusted so as to maintain a sustained beneficial arterial pressure. In most instances, the continuous intravenous drip method of administration is most satisfactory. Combinations of the amines often prove effective when the individual drug has failed to produce the desired result. Although response to customary doses may be absent during prolonged periods of shock, a judicious increment in dosage may be beneficial.

**Methods of Restoring Vasopressor Response**

In spite of treatment, patients with myocardial infarction frequently lapse into a refractory state of chronic shock, in which they may remain for a surprising number of hours before death. This observation has prompted a search for a means of restoring lost response to antishock therapy. C-11 oxysteroids (cortisone) and cholinesterase have been used for this purpose in our investigation, in combination with other measures used to combat shock. Our findings are not in agreement with those in a recent report by Kurland and Freedburg, who noted potentiation of the blood pressure response to norepinephrine within 24 hours of the administration to normotensive subjects of 90 to 180 mg. of adrenocorticotrophic hormone (ACTH) daily, or 150 to 200 mg. cortisone daily. In 12 cases of myocardial shock cortisone was administered as an adjunct medical with no pressor response in 11 patients and very questionable control of shock in one patient.

Cholinesterase was administered in increasing dosage hoping for a pressor effect in 10 patients with myocardial shock. In one case there was a doubtful response while in the other 9 cases there was no response seen.

Table 4 gives a comparison of all measures used to combat shock during the period of investigation, including the administration of cortisone and cholinesterase.

**Conclusion**

The promptness with which anti-shock treatment is instituted is apparently more important than the particular method used. "Routine" measures, venous infusions, retrograde arterial infusions, and the newer sympathomimetic amines are all of value in the treatment of shock associated with myocardial infarction. Cortisone and cholinesterase may be of value in restoring lost responses to antishock therapy.

**SUMARIO ESPAÑOL**

Como un fondo al problema del choque asociado al infarto del miocardio agudo, se han revisado 816 casos recientes consecutivos y comprobados. Ciento sesenta y un casos llenaron el criterio arbitrario para la definición de choque. Demanera que hubo una incidencia de 20 por ciento de choque en los pacientes con infartos del miocardio. La mortalidad fue de 81 por ciento (128 pacientes murieron). En el presente estudio, 134 pacientes con infartos agudos del miocardio en choque fueron tratados. Todos estos pacientes fueron tratados primeramente con medidas puramente rutinarias, incluyendo digital cuando estuvo indicado. Sesenta de los 134 pacientes fueron mejorados con la terapia rutinaria administrada en un período de tiempo de tres horas. Los restantes 74 pacientes fueron tratados con (1) infusión retrograda arterial (2) las nuevas drogas simpatomiméticas como me,
thoxamine, isopropylnorepinephrine y norepinephrine y (3) otros agentes como co-linesterasa y cortisona. Una evaluación de estos métodos se hizo y la mortalidad general del choque asociada al infarto del miocardio se redujo de 81 por ciento a un 48 por ciento.

REFERENCES
The Treatment of Shock Associated with Myocardial Infarction

GEORGE C. GRIFFITH, W. B. WALLACE, BURT COCHRAN, JR., W. E. NERLICH and W. G. FRASHER

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