THE EFFECT OF HYDRALAZINE (APRESOLINE) ON SHOCK

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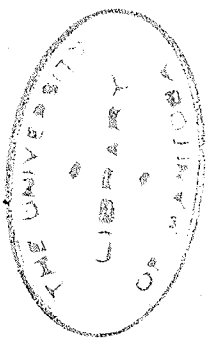

by

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Abstract

Review of the pertinent literature indicates that vasoconstriction and decreased cardiac output result in diminished blood flow to most organs during shock. Impairment of blood supply to vital viscera, especially the liver, may well be responsible for the development of irreversibility to transfusion. Drugs which increase blood flow by interfering with sympathoadrenal vasoconstriction decrease mortality of animals subjected to traumatic or hemorrhagic shock.

In the present study, hydralazine, an agent which increases cardiac output and causes dilatation in the splanchnic area in normal animals and man, decreased mortality of animals subjected to milder, but not those subjected to more severe hemorrhagic or traumatic procedures. In addition, it protected remarkably against acute traumatic deaths due to tumbling, the first demonstration of protection against this type of death by a pharmacological agent.

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CHAPTER I

Introduction *

Numerous definitions of shock have been proposed during the past century. None, however, is entirely satisfactory and their large number reflects the inadequacy of our knowledge and understanding of the problem. Shock remains a general concept or syndrome rather than a well defined entity. It can be precisely recognized only in its advanced stages which are characterized by some as yet incompletely understood event or events leading inexorably to death hours or even days after the end of the period of stress.

In most of its forms, shock may be considered to be a s u b a c u t e, g e n e r a l i z e d c a r d i o v a s c u l a r i n s u f f i c i e n c y. This term differentiates it from chronic conditions such as congestive heart failure, and from acute and subacute impairment of blood supply to localized areas, e.g., due to embolism or thrombosis. It differentiates it further from acute deaths which may result from the same causes which under different circumstances lead to the typical picture of shock. Deaths from acute exsanguination and acute traumatic deaths such as may result from trauma in the Noble-Collip drum (71) fall into this category.

In shock blood flow to most organs is reduced, although the extent of the reduction may differ widely in different vascular beds. The blood supply to some organs may become insufficient for their functional and/or

* The literature, on which the ideas outlined in this introduction are based, is reviewed in some detail in the following chapters. Therefore no references to specific articles are made, except in cases where no further discussion is presented.

metabolic demands and if this inadequacy persists too long, undefined irreversible changes in vital organs may develop. Once this has occurred, recovery will not take place in spite of all treatment presently available and the shock is said to be irreversible.

Although other primary factors may operate, a deficit in the effective circulating blood volume appears to be present early in most forms of clinical and experimental shock including shock due to hemorrhage, burns and various forms of trauma (13,14,15,17,32,59). Various mechanisms may be brought into play by the body in attempts to correct or compensate for this circulatory inadequacy. These may be divided into two main categories:

1) Those tending to increase the circulating blood volume.

2) Those associated with circulating the available blood volume in the most effective manner.

Mechanisms prominent in the first category are: a) discharge of blood from "reservoir areas" such as the spleen, at least in the dog (63), and perhaps other visceral or vascular spaces (42), and b) entrance of fluid from the extravascular spaces into the circulatory system.

The most effective circulation of the available blood volume would be such that each organ would receive just enough blood for its "survival" and for the minimum level of function necessary for survival of the organism as a whole. The requirements of various tissues and organs obviously will vary. In shock the extent of changes in blood flow to various vascular beds also varies, and in any particular area it will depend on:

1) The perfusion pressure or arterial pressure.

2) The resistance to flow offered by the vascular bed in question.

The blood pressure in turn depends on the cardiac output and the total peripheral resistance, the resultant of the resistances of all vascular beds in the body.

The degree to which the vasculature of any organ or tissue participates in the generalized vasoconstriction which occurs in shock will thus be the major factor determining the blood flow to that area, assuming that the blood pressure available to all parts of the body is the same or approximately the same. The great variations in the amount of vasoconstriction occurring in the blood vessels of various tissues in shock probably are due both to differences in the amount of vasomotor innervation and to differences in the responsiveness of the various vascular beds to humoral vasoactive agents. For example, in the skin, where the nerve supply to the blood vessels is rich and where wide fluctuations in the amount of vasoconstriction and vasodilatation occur under physiological conditions, vasoconstriction and reduction in blood flow in shock are marked. Severe vasoconstriction in shock also takes place in some abdominal viscera, e.g., in the kidney and the splanchnic area. In contrast, blood vessels of the heart and brain are supplied with few sympathetic vasoconstrictor nerve fibres, and their blood flow is governed largely by metabolic demands rather than by nervous or humoral constriction. Thus there is less vasoconstriction in the cerebral and coronary vessels and the blood flow is reduced to a lesser degree than in most other areas during shock. In other words, the body tends to maintain blood flow to some organs, such as the brain or the heart, at the expense of others where severe vasoconstriction takes place. This results in a