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Shock Following Myocardial Infarction:

A Clinical Survey of 140 Cases

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ABSTRACT

All admissions for acute myocardial infarction to a metropolitan general hospital over a 10-year period have been reviewed. One hundred and forty patients developed complications meeting the criteria for cardiogenic shock. The mortality rate in this group of patients was 83%. The mortality rate in 95 patients who received treatment with intravenous noradrenaline was no different from that in 45 patients who did not receive this type of therapy ($p = >0.8$). Patients dying from cardiogenic shock were younger than those dying of other complications. Autopsy study of this group of shocked patients revealed a significantly lower incidence of previous healed myocardial infarction ($p = <0.01$).

A decline in the annual incidence of cardiogenic shock was noted over the decade surveyed. It is suggested that this may be due to the earlier and more frequent use of intravenous noradrenaline. Despite the reduction in the incidence of shock, the annual mortality rate from myocardial infarction has remained unaltered.

SOMMAIRE

On a revu les dossiers de patients admis à un hôpital général métropolitain, pour infarctus aiguë du myocarde. Cent quarante cas développèrent des complications diagnostiques de choc cardiogénique. Chez ces patients le taux de mortalité était de 83%. La mortalité parmi 95 patients traités avec noradrénaline par voie intraveineuse n'était pas différente de la mortalité parmi 45 patients chez qui cette forme de traitement ne fut pas employée ($p = >0.8$). Les malades qui moururent de choc cardiogénique étaient plus jeunes que ceux qui moururent d'autres complications. Les autopsies, chez ces patients, démontrèrent une fréquence moindre d'infarctus antérieurs guéris ($p = <0.01$).

Au cours de ces 10 années, on a remarqué une diminution dans l'incidence annuelle de cas de choc cardiogénique et on a suggéré que cette diminution pourrait être attibuée à l'emploi plus fréquent et plus tôt de noradrénaline par voie intraveineuse. Malgré la diminution de l'incidence de choc cardiogénique, le taux de mortalité attribuable aux infarctus du myocarde est demeuré le même.

THE occurrence of circulatory collapse following acute myocardial infarction has long been recognized as a complication of grave prognostic significance.[1, 2] The syndrome, which has been termed cardiogenic shock, may develop within a short interval following the onset of cardiac ischemic pain. The syndrome consists of profound hypotension, pallor, sweating and clouding of the sensorium with coldness and cyanosis of the extremities and weak or absent peripheral pulses.

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Signs of congestive heart failure such as orthopnea, basilar rales and an elevated central venous pressure may be present to a mild degree but are usually conspicuously absent.

The mortality in patients developing cardiogenic shock has been reported by various authors to be between 39% and 100%.[3] This variability may be ascribed to the selection of patients according to differing criteria and, in particular, to the fact that many patients develop transient hypotension following acute infarction without showing evidence of impaired peripheral blood flow. Inclusion of these patients and those with hypotension secondary to transient arrhythmias or oversedation has made difficult an accurate assessment of specific methods of treatment, in particular the infusion of intravenous pressor amines.

Despite the numerous reviews on the subject of cardiogenic shock, little is known of the pathophysiological mechanisms leading to this familiar clinical phenomenon. This is partly due to the difficulties encountered in obtaining detailed hemodynamic observations in critically ill patients and partly because of difficulty experienced in experimentally reproducing the syndrome in animals. Lack of experimental data has thus given rise to considerable speculation concerning the relative importance of the heart and of the sympathetic nervous system in the development of this syndrome.[4]

A further question which remains unanswered is why certain patients develop this complication, and why other infarctions are complicated not by shock but by congestive heart failure or death from sudden arrhythmia. It might be suspected that the more extensive the area of infarction the greater the predisposition to shock. However, no satisfactory correlation has been shown between the extent of infarction and the occurrence of shock.

Finally, the observation that some patients survive relatively long periods of cardiogenic shock, even without the benefit of vasopressor therapy, has stimulated the hope that this syndrome results from a potentially reversible failure of some factor concerned with the regulation of the peripheral circulation or with myocardial function itself.[5] With these questions in mind, it was decided to make a retrospective survey of cardiogenic shock as encountered in a general hospital over a 10-year period.

MATERIALS AND METHODS

The records of all patients admitted to the Montreal General Hospital during the years 1952 to 1961 inclusive with a final diagnosis of acute myocardial infarction were examined. The period 1952 to 1961 was chosen because, although the treatment of uncomplicated acute myocardial infarction did not alter significantly over this period, an alteration in approach to the treatment of cardiogenic shock did occur with the introduction of intravenous pressor-amine therapy. Anticoagulant therapy for control of thromboembolic complications of acute myocardial infarction was firmly established by 1952, while the newer methods of resuscitation and electrical rhythm reversion had not appeared by 1961. It was thus felt that this period provided the best opportunity to make a statistically valid assessment of the therapeutic value of vasopressors in the treatment of cardiogenic shock.

Selection as a case of cardiogenic shock required that each of the following criteria be met: (1) Recent myocardial infarction demonstrated by unequivocal electrocardiographic changes or by subsequent postmortem examination. (2) Protracted hypotension as evidenced by a systolic blood pressure of 80 mm. Hg or less, recorded on at least two consecutive occasions over a period of 30 minutes or longer. (3) Signs of peripheral circulatory inadequacy as manifested by the documentation of two of the following five physical signs: pallor, cyanosis, sweating, cold extremities or clouding of the consciousness. These criteria, which are essentially similar to those adopted by Heyer,[6] are designed to exclude patients with what has been termed "benign hypotension" or "pseudo-shock" in whom signs of circulatory inadequacy are absent and whose hypotension can be related to the effects of drugs or to inaccurate recording of the blood pressure. These criteria are also designed to exclude patients in whom shock is brief and agonal, e.g. following massive pulmonary embolus, myocardial rupture or in the terminal stage of congestive heart failure. Each chart was reviewed for information pertaining to the patient himself, his antecedent medical history, location of the infarction, time of onset and duration of shock, the therapy employed and survival.

A separate pathological study was made of all patients dying with cardiogenic shock who came to autopsy during the last five years of the study. The autopsy protocols of this group, comprising 31 patients, were reviewed and the sections of heart, lungs and kidneys were re-examined. For purposes of comparison, a similar review was made of the records of 31 patients with acute myocardial infarction chosen at random who died during the same period without showing the clinical features of shock.

RESULTS AND DISCUSSION

Clinical Characteristics

A total of 2296 records comprising all admissions for myocardial infarction for the period 1952 to 1961 were reviewed. The sex ratio, mortality and incidence of shock are listed in Table I. Despite the equal availability of male and female beds, male admissions exceeded female admissions in a ratio of 2.5:1.

The age distribution for males and females is shown graphically in Fig. 1. The distribution curves are roughly symmetrical for both sexes but the curve for females is displaced to the right, indicat-

TABLE I.—ADMISSIONS FOR ACUTE MYOCARDIAL INFARCTION, 1952-1961 INCLUSIVE

	Total	*Males*	*% of Total*	*Females*	*% of Total*
No. of admissions for myocardial infarction	2296	1641	71	655	29
No. of deaths from myocardial infarction	677	437	64	240	36
Deaths as % of admissions.....	29.5	26.5		36.7	
No. of patients developing shock....	140	93	65	47	35
Incidence of shock as % of admissions.....	6.1	5.7		7.2	
No. of patients dying from shock....	116	75	65	41	35
Deaths from shock as % of patients developing shock....	82.9	80.6		87.2	
Deaths from shock as % of all deaths.....	17.1	17.2		17.1	

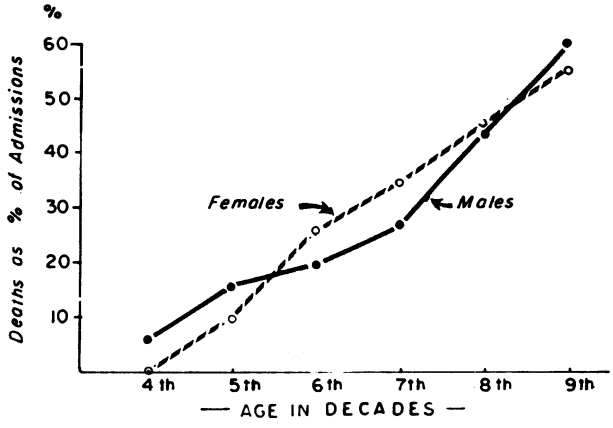

Fig. 2.—Hospital mortality rate for acute myocardial infarction related to age. Data based on 2296 consecutive admissions.

ing a peak incidence approximately one decade later. The peak incidence for males was found to be 58 years and for females 69 years. The annual mortality rate from acute myocardial infarction remained remarkably constant over the period surveyed and was found to be 29.5% overall. Mortality in females was significantly higher than in

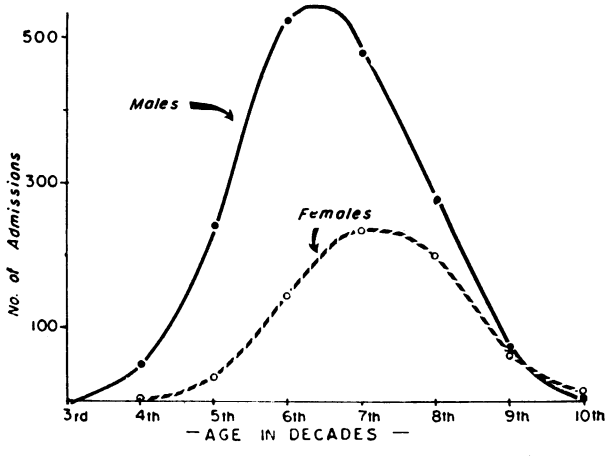

Fig. 1.—Age distribution curves for 2296 cases of acute myocardial infarction in males and females admitted to the Montreal General Hospital, 1952-1961 inclusive.

males, but this could be accounted for on the basis of the greater age of the females, since no significant sex difference was found when mortality was plotted against age (Fig. 2).

One hundred and forty cases, or 6.1% of the total admissions, were found to fulfil the criteria for cardiogenic shock. This incidence is considerably lower than that reported in series in which less stringent criteria for the selection of shock cases were used but approximates the incidence reported by those authors whose criteria were similar to ours.[6] Of interest is the progressive decline throughout the decade in the annual incidence of shock, as shown in Fig. 3. Among the 140 cases of shock, 116 patients failed to survive, indicating a mortality rate of 82.9%. Shock accounted for 17.1% of all deaths from myocardial infarction. No significant sex difference in the mortality rate from shock was found.

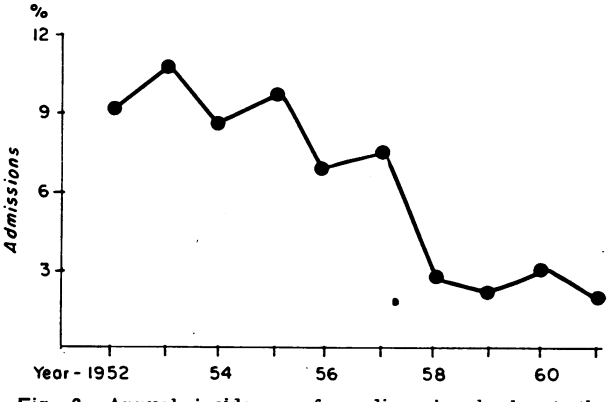

Fig. 3.—Annual incidence of cardiogenic shock at the Montreal General Hospital, 1952-1961. Incidence plotted as percentage of admissions for acute myocardial infarction.

The clinical characteristics of the group of patients developing shock are listed in Table II. It is of interest that the age distribution and average age of this group of patients parallel those

TABLE II.—CLINICAL FEATURES OF 140 PATIENTS DEVELOPING SHOCK AFTER MYOCARDIAL INFARCTION

	Males	*Females*	*Total*	*Survivors*
No. of patients	93 (65%)	47 (35%)	140	24 (17%)
Age range (years)	32-80	50-88	32-88	46-88
Average age	59.2	68.6	63.0	60.1
History of previous myocardial infarction			45 (32%)	6 (25%)
Location of infarction by ECG or autopsy				
Anterior or anterolateral			80 (57%)	11 (46%)
Posterior or posterobasal			60 (43%)	13 (54%)
Average interval between admission and onset of shock (hours)			18.2	
Average duration of shock (hours)			20.4	20.2

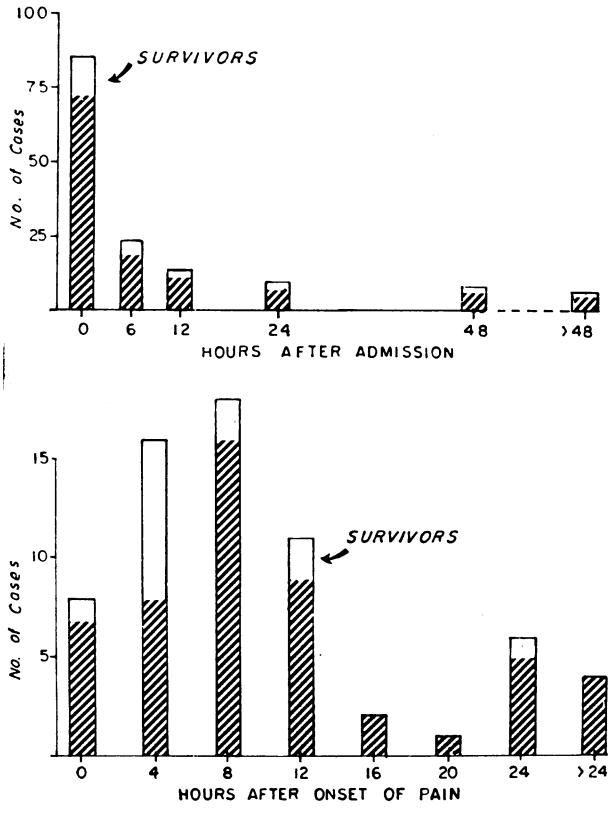

Fig. 4.—Upper: Interval between admission to hospital and appearance of cardiogenic shock in 140 cases. Lower: Interval between onset of cardiac ischemic pain and appearance of shock in 66 patients admitted to hospital in shock. Unshaded area in each column of the histograms indicates the patients who survived.

for myocardial infarction as a whole, rather than for those patients dying from myocardial infarction. The average age of patients dying from cardiogenic shock was thus four years younger than those dying from all complications of infarction. This finding is in contrast to those of others who have suggested that advancing age is a predisposing factor in the development of fatal cardiogenic shock. The ratio of males to females among the shock patients was not different from that for myocardial infarction.

It has been reported by others that cardiogenic shock is more prone to develop in patients who have previously experienced one or more infarcts.[7] We were not able to confirm this observation, since only 32% of the shock patients gave a history of previous myocardial infarction. Neither did prior infarction influence mortality, since six out of 24 patients survived an episode of cardiogenic shock complicating a second myocardial infarction.

The location of the infarction in patients developing shock as determined by the electrocardiogram or at subsequent necropsy showed an approximately equal distribution between anterior and posterior infarctions.

Shock was present on admission to hospital in over one-half of the cases surveyed (Fig. 4). It was possible to determine the interval between the onset of cardiac ischemic pain and the occurrence of shock in 66 of the 85 patients who were admitted in shock. Shock accompanied the onset of pain in relatively few patients; in most cases it appeared after an interval of several hours. This latent interval between the occurrence of pain with electrocardiographic evidence of myocardial infarction and the onset of shock has been remarked upon by several authors reviewing the subject, and no satisfactory explanation has yet been offered. In a few patients, shock as a complication did not develop until 24 hours or more after admission to hospital and in this group it may have been related to extension of the myocardial infarction. The average interval between the onset of pain and the occurrence of shock was 8.5 hours in the group admitted in shock. In the remainder, shock appeared, on the average, 18.2 hours after admission.

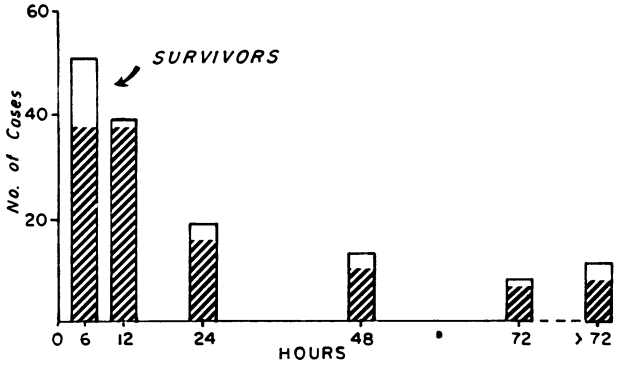

Fig. 5.—Duration of shock in 140 consecutive cases of cardiogenic shock. The shaded area of each column indicates the number of fatal cases and the clear area the number of survivors.

The average duration of shock was 20.2 hours in those surviving this complication and 20.4 hours in the 116 patients who died (Fig. 5).

It has been suggested that hypotension which lowers coronary perfusion pressure is especially liable to provoke a fatal arrhythmia following acute myocardial infarction by increasing myocardial hypoxia.[8] It is of some interest that two-thirds of the 116 patients dying from cardiogenic shock were able to tolerate a period of shock in excess of six hours before death ensued. Owing to the hypotension and low cardiac output, left ventricular work is markedly reduced in shocked patients and myocardial oxygen requirement is lower. It is possible that lowered coronary perfusion is offset by a lower oxygen demand and that the oxygen requirements of the non-infarcted myocardium are satisfactorily met even during periods of severe hypotension. It is conceivable that death from cardiogenic shock may be related as much to impaired peripheral blood flow and metabolic changes secondary to hypoxia in organs other than the heart as to myocardial hypoxia itself.

Treatment

During the decade covered by this survey, a striking change was observed in the therapeutic approach to cardiogenic shock. In the earlier years of the study, rest, sedation and oxygen were frequently the only treatment accorded to patients with cardiogenic shock although some patients received saline infusions, blood transfusions or subcutaneous phenylephrine. Parenteral digitalis preparations were given to only 10% of patients. Intravenous noradrenaline, which became available during the period covered by this study, was used with increasing frequency, every patient reviewed during the final four years of the study having

TABLE III.—EFFECT OF INTRAVENOUS NORADRENALINE IN 140 CASES OF SHOCK

	Treated with I/V noradrenaline	*Not treated with I/V noradrenaline*
Number of cases....	95	45
Satisfactory pressor response....	47 (50%)	
Survived.....	16 (17%)	8 (18%)
	$\chi^2 = 0.0207$	
	$p = > 0.8$	

received this drug. Although this drug was originally believed to exert a pressor effect by increasing peripheral arteriolar resistance, it has been shown that in patients who respond satisfactorily to this agent, peripheral resistance is usually diminished rather than increased. It is now known that its principal action, when given in low dosage, is to increase cardiac output by enhancing myocardial contractility.[9] Despite the proved positive inotropic effect of intravenous noradrenaline, some controversy exists concerning its therapeutic value in the treatment of clinical cardiogenic shock. In the series of patients under review, 95 received intravenous noradrenaline, of whom 17% survived. Of 45 untreated patients, 18% survived. Despite the fact that noradrenaline was able to elevate the systolic blood pressure to 90 mm. Hg or greater in 50% of the patients treated with this drug, no significant difference in the mortality rates was noted between patients treated with this drug and those who were not (Table III). At the present time, when intravenous noradrenaline infusion is so uniformly used in the treatment of cardiogenic shock, it is sometimes forgotten that patients occasionally survived periods of profound shock without the application of any specific pressor therapy. Fig. 6 summarizes the clinical course of such a patient who became severely shocked 20 hours following an acute myocardial infarction.

The patient, a 57-year-old woman, was hypotensive for 24 hours, the arterial blood pressure being unobtainable by cuff for four hours. She was described by her attending physician as appearing "gravely ill with ashen grey colour; pulse and blood pressure unobtainable; heart

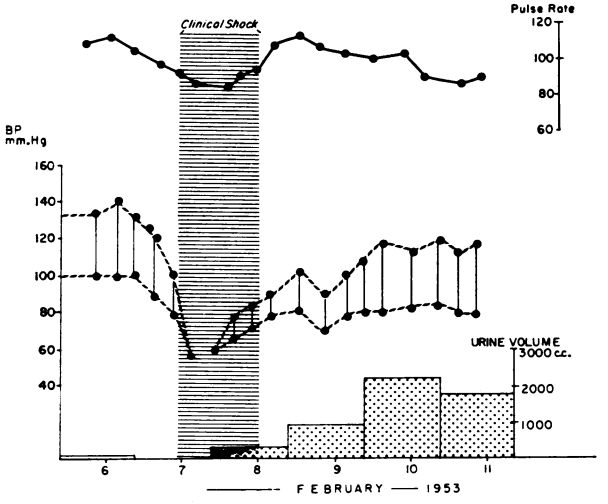

Fig. 6.—Clinical course of a 57-year-old woman, admitted with acute myocardial infarction, who survived an episode of severe cardiogenic shock and did not receive vasopressor therapy.

sounds inaudible". The patient was treated with rest, oxygen and anticoagulants, no pressor agents being used. After 24 hours the blood pressure slowly increased and the patient's clinical condition improved; she was discharged to her home four weeks later, the remainder of her course in hospital having proved uneventful.

The earlier and freer use of intravenous noradrenaline may have played a part in the gradual

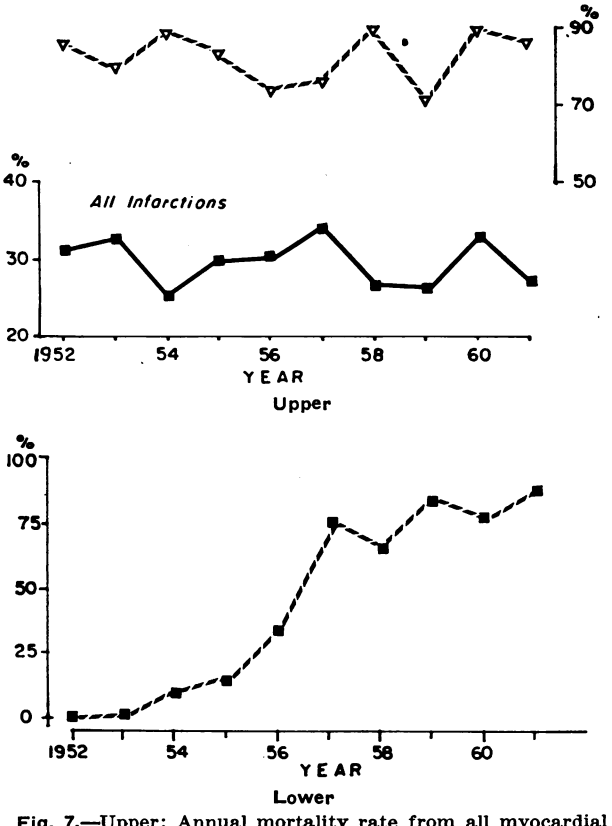

Fig. 7.—Upper: Annual mortality rate from all myocardial infarctions and from those complicated by cardiogenic shock. Lower: Yearly percentage of cases of cardiogenic shock receiving intravenous noradrenaline in dosage greater than 10 μg./min.

TABLE IV.—COMPARISON OF AUTOPSY DATA IN 31 PATIENTS DYING IN SHOCK FOLLOWING MYOCARDIAL INFARCTION WITH DATA FOR 31 PATIENTS DYING OF OTHER COMPLICATIONS

	No. of patients dying in shock	*No. of patients dying from complications other than shock*	*Significance*
HEART			
Weight < 450 g...	21	19	NS
Weight > 450 g...	11	13	NS
Recent infarction.	27	24	NS
Healing or remote infarction.....	15	25	Highly significant ($p = < 0.01$)
LUNGS			
Weight < 750 g...	20	18	NS
Weight > 750 g...	11	13	NS
Hyperemia.....	25	29	NS
Edema.....	27	31	NS
Chronic passive congestion or heart failure cells.....	21	22	NS
KIDNEYS			
No evidence for renal shutdown (tubular necrosis).	21	19	NS
Suggestive evidence for renal shutdown	7	8	NS
Definite evidence for renal shutdown	3	4	NS

decline observed in the annual number of patients developing cardiogenic shock during this 10-year survey. In 1952, 9.2% of admissions for myocardial infarction developed this complication, whereas in 1961 the incidence had fallen to 2.8%. In view of the high mortality rate in cardiogenic shock, a reduction in the incidence might be expected to cause a reduction in the overall mortality rate from myocardial infarction; however, no such reduction was observed (Fig. 7). It is possible that with the earlier and freer use of intravenous noradrenaline, especially in higher dosage, the arterial pressure of patients who might have developed the criteria for shock was not permitted to drop to 80 mm. Hg and these patients did not come to light in the survey. The fact that the overall mortality did not alter significantly over the whole period of the study is further evidence that the more widespread use of noradrenaline, while controlling the principal feature of cardiogenic shock, i.e. hypotension, has not significantly altered the mortality.

Autopsy Findings

The autopsy protocols of 31 patients dying during the last five years of the survey period were reviewed and compared with the protocols of a similar number of patients admitted with acute myocardial infarction but dying of complications other than cardiogenic shock. All of the 31 shock patients received intravenous noradrenaline. Particular attention was paid to gross and microscopic findings in the lungs, heart and kidneys. A summary of the data obtained is listed in Table IV.

It has been argued that the primary factor responsible for cardiogenic shock is impaired contractility of the injured myocardium, and the syndrome has been regarded as a fulminant form of left ventricular failure.[10] This explanation has not been supported by the limited hemodynamic data available from clinical studies, in particular the finding of a normal or near-normal central venous pressure.[11] In our series it can be seen that comparison of lung weights and of microscopic evidence of acute and chronic pulmonary congestion revealed no significant difference between the group dying with shock and the group dying of other causes. In both groups the appearance of those features was related solely to the interval between infarction and death. This evidence corroborates the work of Malach and Rosenberg,[7] and suggests that the clinical syndrome of shock, at least at its onset, is not related to left ventricular failure alone. This hypothesis is further supported by hemodynamic studies in experimental animals in which left ventricular filling pressure was found to be only slightly elevated in animals in profound shock produced by diffuse coronary embolization.[12]

The sole significant difference between the two groups was revealed during comparison of gross and microscopic findings in the heart. Although heart weight and the incidence of recent infarction were comparable in both groups, the group of patients dying in shock showed a lower incidence of previous, healed myocardial infarction which was significant at the 1% level. This finding is in keeping with the less frequent history of previous myocardial infarction in the group of patients with cardiogenic shock reported here, and both these observations suggest that the occurrence of previous myocardial infarction has a protective effect. In any event, the complication of cardiogenic shock is less likely to develop in those with a clinical history or other evidence of previous myocardial infarction. Possibly the development of collateral channels between main coronary trunks, which is known to be promoted by coronary occlusion, is a factor which inhibits the development of this particular complication.

Evidence of acute renal shutdown, as judged by histological evaluation of kidney sections, was found no more frequently in those patients dying from shock than in those dying from other complications. Since all patients dying from shock were treated with intravenous noradrenaline, it does not appear that noradrenaline increases the hazard of this additional complication, although it should be noted that the pathological diagnosis of this condition is a subject of some controversy.[13]

SUMMARY AND CONCLUSIONS

All admissions for acute myocardial infarction to a metropolitan general hospital over a 10-year period have been reviewed. One hundred and forty patients

developed signs and symptoms fulfilling the criteria for cardiogenic shock. The mortality rate in these patients was 82.9%, compared to 29.5% for myocardial infarction as a whole. Fatal cardiogenic shock has been shown to develop in patients having a lower average age than those dying of other complications. Patients dying of cardiogenic shock also had a less frequent history of antecedent coronary thrombosis and at autopsy showed a significantly lower incidence of healed infarction. No difference with regard to sex or location of the infarction could be discerned in the shock group. Survival in those patients developing cardiogenic shock who were treated with intravenous noradrenaline was not significantly different from those who did not receive this type of therapy. The declining incidence of this complication is noted and it is suggested that this may be associated with the freer use of intravenous pressor agents, although this therapy does not appear to have altered the overall mortality from myocardial infarction.

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Cancer Mortality Trends in Canada—1944-1963

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ABSTRACT

A 20-year statistical review was undertaken to ascertain significant changes in cancer mortality in Canada by site and sex. Cancer in nine major sites and leukemia were studied. Trend lines were fitted to the death rates and the probability was computed that the slopes of these lines had changed significantly. Of the 17 analyses made, significant decreases in mortality were found in six and significant increases in six. In the remaining five analyses no significant change in mortality was found.

SOMMAIRE

Une étude statistique d'une durée de 20 ans a été entreprise pour savoir si des fluctuations notables de la mortalité par cancer étaient survenues durant cette période, en ce qui concerne son siège et le sexe affecté. Après adaptation de ces courbes particulières aux courbes de la mortalité générale, on a calculé la probabilité d'un changement notable. Des 17 études analytiques effectuées, six révélaient une sensible diminution et six une nette augmentation. Les cinq dernières analyses ne révélèrent aucun changement de la mortalité.

THE analysis of mortality data has contributed greatly to the development of cancer epidemiology. An early and notable example was the examination of death certificates in the Schneeberg district of Saxony which revealed the high lung cancer risk among the miners in that area. Many other occupational and social class differences have been described and, more recently, mortality data have indicated important differences in trends for specific sites, for example, the rise in lung cancer among males, the decline in gastric cancer in both sexes, and the unchanged rates for female breast cancer. The more detailed data from cancer morbidity surveys and registries have been found, in many respects, to be consistent with inferences based on mortality data. However, while these special studies have resulted in greater specificity in inquiries into cancer epidemiology and have served purposes that cannot be adequately met by mortality statistics, they are restricted in both space and time. For geographic comparisons or for the analysis of long-term trends, therefore, it is still necessary to rely on mortality data. The diagnostic uncertainties inherent in the medical certification of death have given rise to the vexing question of what part of the recorded mortality trend is actually real. In Canada, a study[1] of some 7000 cancer deaths indicated that the over-diagnosis of cancer amounted to 11.0% and was found, mainly, in relation to the stomach and pancreas. On the other hand, the under-diagnosis of cancer was 5.9% and

A more extensive report showing mortality trends for each province is available upon request from the National Cancer Institute of Canada, 790 Bay Street, Toronto 2, Ontario.

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