

PRE-HOSPITAL DEATHS DUE TO ISCHAEMIC HEART DISEASE IN SINGAPORE

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Death due to Ischaemic Heart Disease (IHD) is the leading cause of death in most developed countries, forming up to a third of all causes of death (WHO Statistics). In Singapore, deaths due to IHD had increased throughout the years. In 1959, it formed 4.2% of the total deaths, but in 1971, this had increased to 8.2% of all deaths. In some of these cases, death occurred suddenly and unexpectedly outside the hospital, and unless the family physician could certify death, these cases were referred to the Coroner. The Coroner's autopsy rate was about 55%, the rest of the cases reported would be certified by the Coroner without an autopsy. Of the autopsied cases, 70% were due to unnatural deaths, and 30% natural deaths. A third of the natural deaths were due to IHD, many were brought in dead, died on arrival at hospital, or died soon after admission. A study was made of 191 such cases in the three-year period 1969, 1970 and 1971, from autopsy protocols, police reports, interview with relatives and information from general medical practitioners who had been looking after these cases; to assess the presence of premonitory symptoms, pre-disposing factors, and the ethnic, age and sex patterns. As it was intended to study the pre-hospital phase of IHD deaths, cases that died after operation and admitted for more than five hours in hospital were excluded. Included were 7 patients from mental institution, 2 from leprosarium and 2 prisoners, as they were not treated for heart disease in their places of detention but suddenly died of IHD. This series represented 7% of the total number of deaths due to IHD recorded at the Registry of Births and Deaths of Singapore during the period (total number 2607).

Present Study

Cases that died of IHD in this series were all above 30 years of age. There were 169 male cases and 22 female cases giving a male to female ratio of 7.7:1. The majority of the cases fell in the 4th and 5th decades (Table I). This was in general agreement with other reported series (Adelson and Hoffman, 1961). The ethnic groups showed 54% Chinese, 26% Indians and Pakistanis, 6% Malays and 14% of other races (Table II). The population composition of Singapore was 74.4% Chinese, 7.9% Indians and Pakistanis, 14.5% Malays and 3.2% other races. Therefore, the Indians and Pakistanis appeared to have a higher risk than other cases of sudden deaths due to IHD.

Forty-five cases were found dead and therefore the onset of symptoms were unwitnessed. In the remaining 146 cases, the attack was witnessed by friends or relatives. Of these 106 cases or 72.6% collapsed and died within one hour of the onset of symptoms, in fact, the vast majority of them died within the first 15 minutes. In all, 95% of the witnessed cases died within 24 hours of onset of symptoms. There were 7 cases that survived more than 24 hours and up to 46 hours, the delay was due to self-medication or treatment by traditional Chinese herbal medicine before they finally seek help from the hospitals (Table III).

Looking into the activities immediately before death from the police reports, 21 of them were manual workers who had collapsed at work (Table IV). They were doing heavy manual work such as loading and unloading cargo, moving logs or in building construction work. Seven of them died immediately after quarrels, fist fights or slumped at the wheel in traffic accidents. But the majority of them had low activity before death. Thirty-six had mild exertion in the form of walking, doing light work and washing. Twenty-five of them had no exertion at all when they collapsed at reading, watching television or film show and on

going to bed. Enquiries were made into their activities in the last 24 hours and showed no exceptional stress and strain but followed the daily routine. There were 10 tourists who flew in to Singapore for a visit, 2 of them died in the aircraft, 1 at the embarkation hall, the rest in hotels. However in 6 cases there was history of previous heart disease of hypertension, and these were confirmed with the medical practitioners who had been looking after them. Besides those that died in the air, there were 8 cases of deaths at sea; they included passengers and officers on board ships. Previous history was unobtainable in these cases because of lack of information. Of interest were 8 cases that died after sexual intercourse. They were all above 45 years of age and were able to complete the sexual act but collapsed later while resting and smoking a cigarette or washing in the bathroom. These were illicit love affairs and their partners were either prostitutes or mistresses. However, these cases were evident because they were all reportable to the coroner. Cases that died in detention included 7 in mental institutions and 2 in prisons. In the rest of the cases they were either unwitnessed or activities not known.

Post-Mortem

As these cases came to the mortuary usually without any clinical history or investigations, pathological findings had to be relied on for the diagnosis of myocardial infarct and coronary artery disease. In all of these cases a complete post-mortem was performed. There were insignificant findings in other systems of the body but the pathology was mainly in the heart. The coronary arteries were examined by cross section at 1 mm. intervals from the origin of the branches. It was found that fresh thrombus occurred in 29 cases or 15%. It would support the concept that coronary arterial thrombus are results rather than causes of myocardial infarction (Roberts, 1972). In 70% of the cases all three branches of the coronary arteries were occluded by atheromatous plaques, and in 10% two branches were involved, in 20% of the cases only one branch was involved, most frequently, the anterior descending branch with severe narrowing by atheromatous plaques of more than 75% occlusion and many with organised thrombus. Six cases had haemorrhages into atheromatous plaques.

The myocardium was then examined for infarcts. As most of these cases died within an hour after the onset of symptoms, gross changes in the myocardium at this stage was not readily discernible except for 11 cases or 6% where the heart was ruptured. More definite changes such as gross haemorrhages and a reddish discoloration occurred at a later stage after about 6 hours, and a yellowish discoloration occurred much later at 24 or more hours. Likewise, microscopic examination by the ordinary Haematoxylin and Eosin stains revealed little changes in the very early infarcts.

However, close examination of the myocardium showed that the earliest naked eye changes in infarcts was oedema and swelling of the myocardial fibres resulting in the swelling and separation of the myocardium fibres giving a coarse appearance as opposed to the smooth glistening surface of the myocardium. This occurred within an hour of onset of symptom. The consistency was soft. Blocks of tissue approximately 1 cm square and 3 mm. thick were cut from these areas with a control block of tissue from a normal area usually from the right atrium. These blocks were unfixed and quickly frozen by carbon dioxide. These were stored at -20°C until required for cutting. Sections were cut in a cryostat at 8-10 microns, picked up by cover slips, air dried for 5 minutes and then incubated at 37°C for about 30 minutes in a histochemical stain to demonstrate activities of Malate Dehydrogenase (MDH).

Histochemical Technique

MDH is a mitochondrial enzyme of the electron transfer chain. It activates specific hydrogen atoms of the

TABLE I
AGE, SEX AND ETHNIC DISTRIBUTION

	Male					Female					Total
	Chinese	Indians & Pakistanis	Malays	Others	Sub-Total	Chinese	Indians & Pakistanis	Malays	Others	Sub-Total	
30 - 39 years	8	3	1	2	14	2	—	—	—	2	16
40 - 49 years	15	18	6	12	51	—	—	—	1	1	52
50 - 59 years	27	12	4	4	47	4	—	—	—	4	51
60 - 69 years	25	10	1	5	41	7	2	—	—	9	50
Above 70 years	10	5	—	1	16	6	—	—	—	6	22
TOTAL	85	48	12	24	169	19	2	—	1	22	191

Male : Female = 169 : 22 = 7.7 : 1

TABLE III
SURVIVAL TIME AND RELATION TO PREVIOUS HEART ATTACKS

		%	History of previous heart attack
Found dead	45	—	—
Less than 1 hour	106	72.7	11
1 - 5 hours	21	14.4	2
5 - 24 hours	12	8.2	2
24 - 46 hours	7	4.8	—
TOTAL	191	100.0%	15 (8%)

TABLE II
ETHNIC GROUPS

Chinese	-	-	-	104	54%
Indian and Pakistanis	-	-	-	50	26%
Malay	-	-	-	12	6%
Others	-	-	-	25	14%
				191	100%

TABLE V

OCCUPATIONS

No employment	-	-	-	90	47%
Manual Labourers	-	-	-	28	15%
Clerks, shop-keepers, office workers	-	-	-	18	9%
Doctor, managers	-	-	-	5	3%
Tourists	-	-	-	10	5%
Ships' officers and workers	-	-	-	8	4%
Patients in institutions	-	-	-	9	5%
Prisoners	-	-	-	2	1%
Unknown	-	-	-	21	11%
TOTAL				191	100%

TABLE IV
CIRCUMSTANCES BEFORE DEATH

Collapse at work	-	-	-	-	21
After quarrel, fight and in traffic accidents	-	-	-	-	7
Mild exertion	-	-	-	-	36
No exertion	-	-	-	-	25
Tourists	-	-	-	-	10
Died at sea	-	-	-	-	8
Died after sexual intercourse	-	-	-	-	8
Patient of mental institution	-	-	-	-	7
Prisoner	-	-	-	-	2

substrate and catalyses their transfer to a hydrogen acceptor—a tetrazolium salt, in this case Nitro-Blue Tetrazolium. It is then reduced to a coloured water-insoluble formazan granule. Cyanide is used to block the reaction to carry on to completion through the cytochrome system.

The following stock solutions were prepared:

1. Substrate 1.0M L-Malic Acid brought to pH 7.0 by addition of solid Tris buffer. Stored frozen.
2. NaCN 0.1M adjusted to pH 7.0 by N HCl. Stored at 0-4°C.
3. Phosphate buffer 0.06M at pH 7.0. Stored at 0-4°C.
4. Nitro-Blue Tetrazolium 1 mg. per ml. Stored frozen.
5. NAD.

A working solution of 20 ml. was prepared from:

Malic Acid	2.0 ml.
NaCN	2.0 ml.
Phosphate buffer	5.0 ml.
Nitro-BT	5.0 ml.
Distilled water	6.0 ml.

After mixing all these solutions then NAD 300 mg. was added. The pH was adjusted to 7.0 and stored frozen.

When required, the working solution was thawed and dropped with a dropper on to the cover slip containing the section until the whole section was covered and incubated at 37°C. This was a more economical and convenient way than the method mentioned by Knight (1965, 1968).

In normal myocardium, sites of activities of MDH were demonstrated by the deposition of blue formazan granules along the myocardial fibres which was uniform in distribution. In infarcted areas where mitochondria were destroyed and the enzymes leaked out there would not be any deposits. Infarcts under one hour's duration would show a patchy loss of the enzymes (Fig. 1). On higher magnification the enzyme loss was shown to be limited at the intercalated disc (Fig. 2). In the infarcts of longer duration the loss was more definite. However, there seemed to be survival of the myocardial fibres around capillaries and immediately below the endocardium due to micro-diffusion of oxygen (Fig. 3). Of course, there were times when the infarct appeared older than the time of onset, but by and large, the distribution of formazan deposits gave a good indication of the duration of the infarct. There was a macro method using whole heart slices of about 1 cm thickness and incubated in Triphenyl-Tetrahydro-tetrazolium Chloride (TTC) or Nitro Blue Tetrazolium to indicate the gross areas of infarct by absence of staining, but the results could be erratic and not always completely reliable. The micromethod was more reliable and results reproducible.

A control series of 20 cases from males of ages 40-60 years who died of other known causes of accidental deaths without previous known heart disease and had no infarcts at post-mortem were examined and no such changes were observed. Therefore this method is satisfactory in the demonstration of early myocardial infarcts.

In the present series 171 cases were examined by the micro-method, which was found reliable up to 48 hours after death, but once decomposition had set in it was no longer reliable. In the remaining 20 cases the staining was not carried out for various reasons. Of the cases examined, 55% had infarcts involving the posterior septal region sometimes with extension to the posterior wall of the left ventricle. Thirty-eight percent of the cases had anteroseptal infarcts with 7% of involvement of the lateral wall of the left ventricle. This concurred with the observation that in autopsy of sudden deaths, infarcts were more commonly found in posterior region (Mottenen, 1970).

Prodromal symptoms, previous disease and smoking habits

From police reports and interviews with relatives, certain prodromal symptoms and previous diseases were revealed. It was found that 29% had acute chest pain before death. Eight percent or 15 cases had history of one or more heart attacks before the fatal episode. All these were confirmed by E.C.G.s obtained from the records of the hospitals



Fig. 1. Malate Dehydrogenase stain X 500. Note the patchy loss of enzyme staining in myocardial infarct.

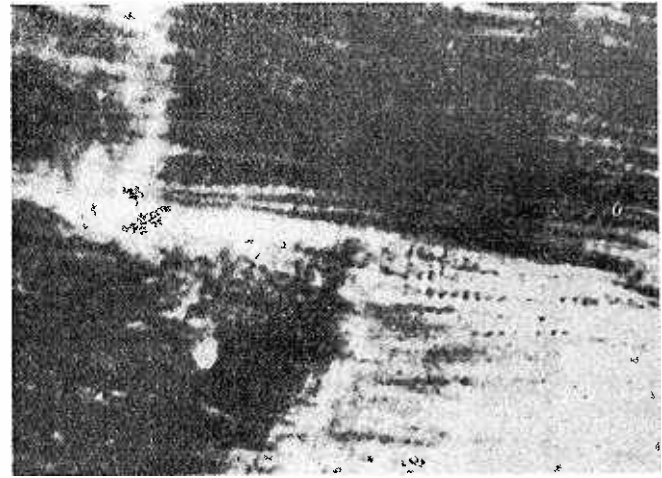


Fig. 2. Malate Dehydrogenase stain X 1,200. Shows the loss of enzyme stops at intercalated disc.

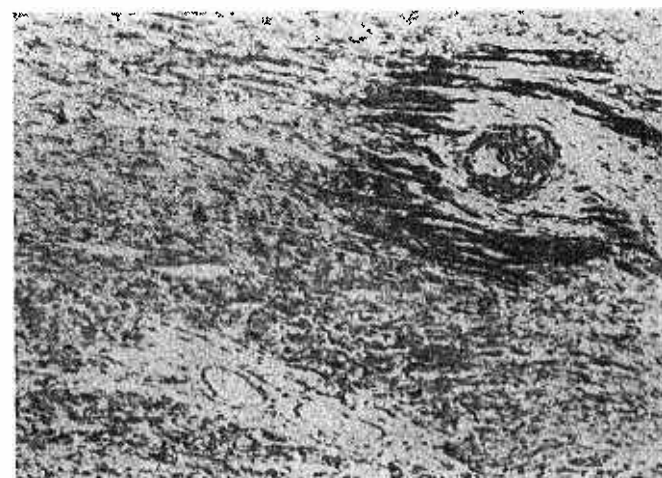


Fig. 3. Malate Dehydrogenase Stain X 75. Shows perivascular enzyme survival in myocardial infarct.

where they were admitted or from the medical practitioners who had been looking after them. Eight of these cases showed anterior infarcts, 6 posterior infarcts, 1 posterior infarct with septal involvement. Seven percent had Diabetes Mellitus and 10% had hypertension. Fifteen percent of these cases had seen a doctor one week before death.

Fifty-eight percent of the cases were smokers of cigarettes of different severity. Nine percent were heavy smokers of more than 30 a day for more than 5 years, 38% moderate smokers of 10-30 a day for more than 5 years, and 11% of light smokers of less than 10 a day for more than 5 years. Non-smokers comprised 13%, in 29% of cases the smoking habit was not known.

DISCUSSION

The cases in this series were selected in that they comprised only of autopsied cases of sudden deaths that were reported to the coroner. Nevertheless, it supplemented the cases seen clinically. It is significant that the majority of these cases had no symptoms of heart diseases before their death, a positive history was obtained in only 8% of the cases, half of them were from visitors abroad. Another 15% of the cases had seen a doctor before death, however exact history of these were not available. These factors were lower than those found in the Baltimore series (Kuller *et al.*, 1966, 1967, 1969). Other known risk factors were not obvious in this series. Only 23% were overweight when compared with the standard height and weight chart for Asians. 74% were normal or underweight. In 3% the height and weight were unknown. Forty-seven percent had no gainful employment, and 15% were manual labourers. The more sedentary workers such as clerks, office workers occupied only 9% and doctors and managers 3% (Table V). This observation is contrary to the impression that HD affected mainly the executive and professional class. The

majority of them had mild or no exertion before death (Table IV), smoking habits were difficult to elicit because of a large proportion of unknown cases. Likewise, the history of previous diseases such as Diabetes Mellitus and Hypertension, was difficult to obtain from relatives. Death was fairly rapid as shown by the 72.6% who died within the first hour of onset of symptoms. Therefore, resuscitation must be at hand, and the setting up of a mobile coronary care unit would be timely. There appeared to be other risk factors involved besides the conventional known ones such as obesity, sedentary work, lack of exercise, etc. and these should be further identified for an effective Primary Prevention Programme. Death from IHD is definitely on the increase in Singapore, this should be halted before it reaches the mortality rate of the highly industrialised countries.

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