Pulmonary Function Following Acute Coronary Occlusion in Dogs[1] (36343)

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The onset of myocardial infarction in man can be accompanied by a multitude of symptoms of which dyspnea is the most frequent. In a reported study of symptomatology 95% of the patients had dyspnea following the first attack of myocardial infarction and 96% following the second attack (1). The mechanism of dyspnea is not well understood at present. Unfortunately, the pulmonary function immediately following myocardial infarction or acute coronary occlusion remains unexplored (2).

In the few clinical studies reported, arterial hypoxemia was observed following the episode and was found to be more pronounced in cases complicated by shock and pulmonary edema (3–6). The arterial hypoxemia could not be due to hypoventilation, since the simultaneously obtained $P_{a_{CO_2}}$ values were neither normal or subnormal. In the cases reported in the literature there is no information on the time lapse between the onset of attack and the laboratory investigation. The object of our present study is to investigate the alterations of pulmonary gas exchange in an animal model from the very onset of acute coronary occlusion. Myocardial infarction has been induced in animals by various ways. These include chronic supplemental dietetic regime, open chest coronary artery occlusion either by ligation or by ameroid constrictors, drugs, and by closed chest occlusion. Methods involving thoracotomy require extensive postoperative care and have high mortality rates. Additionally, the need for positive pressure breathing during the open-chest period makes the method unsuitable for studies on respiration immediately after coronary occlusion. To obviate these drawbacks a modification of the Agress and coworkers' technique (7) has been developed by us for the production of myocardial infarction in closed chest animals (8). This animal model has been found by us to be relatively nonfatal and ideal for various physiologic studies.

Methods. Eighteen beagle-type mongrel male dogs weighing from 7 to 16 kg were anesthetized with intravenous sodium pentobarbital with an initial dose of 30 mg/kg and supplemented as indicated. Endotracheal intubation was performed; and the dogs were permitted to breath ambient air spontaneously. Indwelling polyethylene tubing (PE 190) (filled with heparinized saline) located in the femoral artery was used to monitor systemic blood pressure and to obtain arterial blood samples for analysis. A 0.025 in. Teflon-coated radiopaque catheter (Cook, Inc., U.S.A.), filled with heparinized saline was introduced into the left common carotid artery for coronary catheterization. The carotid arterial catheter was advanced into the ascending aorta and then to the left coronary artery under fluoroscopy and aided by injection of Renografin-60 (Squibb, U.S.A.). The catheter was advanced and manipulated with the aid of the dye into the left coronary artery.

The standard EKG leads were recorded on a Grass model 5 recorder. The femoral artery catheter was connected to a P23AC pressure transducer (Statham, Puerto Rico) filled with heparinized saline; and the pressures were recorded on the Grass recorder. An 18-gauge needle on the end of a rubber tube was inserted in the endotracheal tube and

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attached to the analysis head of a previously calibrated Godart infrared capnograph (Instrumentation Associates, Inc., U.S.A.), which in turn, was connected to the Grass recorder. Simultaneous control values were obtained and recorded: the capnograph for measuring the end-tidal carbon dioxide concentration and respiratory rate; the standard EKG leads for calculating the heart rates, and the pressure transducer for measuring systemic blood pressure. Arterial blood samples were drawn in a heparinized syringe anerobically for measurement of respiratory gas tensions.

Immediately after localization of the catheter in the coronary artery, a small amount (10–15 mg) of polystyrene microspheres (429 to 595 μ, Dow, U.S.A.) suspended in 0.25 to 0.5 ml of isotonic saline was injected. Frequently, the microspheres were further diluted to 2 ml in a plastic syringe with Renografin. This entire procedure was verified by the fluoroscope. We estimate that less than 5 mg of the microscopheres entered the coronary arteries since most of the microspheres remained in the syringe and the catheter.

The heart rate, EKG, blood pressure, and respiratory rates were continuously monitored on the Grass model 5 multichannel recorder before, during, and after introduction of the microspheres. An arterial blood sample was obtained for blood gas analysis from the femoral arterial catheter before and within 1 min after the embolization. The EKG and serum enzyme changes following microsphere embolization technique have been previously reported (8). Blood samples were also taken at various time intervals for serum enzyme determinations; these included SGOT, CPK, and LDH.

All arterial blood samples were analyzed for arterial oxygen tension ($P_{a_{CO_2}}$) and carbon dioxide tension ($P_{a_{CO_2}}$) within 1–2 hr after they were drawn. The samples were analyzed in duplicate on a Beckman model 160 physiological gas analyzer with constant temperature modular cuvette. The electrodes were calibrated with varying known gas mixtures just prior to analysis. The cuvette contained two stacked modules, one housing a Clark oxygen macroelectrode and the other a Severinghaus carbon dioxide macroelectrode.

Production of coronary occlusion leading to myocardial infarction was confirmed by EKG changes and routine enzyme studies and subsequently by postmortem examinations. Only animals showing evidence of infarction are described in this paper. Five of these 18 animals were followed for 2 days following postinfarction period.

Results. All the variables were recorded simultaneously and continuously for 1 hr after infarction was induced. The postinfarction data were divided into two groups: immediate (up to 3 min postinfarction) and delayed (10–60 min postinfarction). All the simultaneous data of the measured variables were available during the first 3-min period. The values described under "delayed" category represents the average values during the 50-min period. The selection of 10 to 60 min as the "delayed," though made arbitrarily, was suggested by obvious differences from the preceding groups. The postinfarction data were statistically analyzed by t test against their own controls. Table I shows the means and standard deviation values of the measured parameters.

There was marked tachypnea immediately following acute coronary occlusion which was highly significant ($p < .005$). This tachypnea persisted for at least 1 hr. Significant systemic hypotension was another noticeable finding ($p < .005$). The systemic hypotension, like tachypnea was more marked during the initial postinfarction period. Tachypnea and systemic hypotension were associated with significant changes in arterial blood gas tensions which were more marked during the initial postinfarction period. There were no significant changes in heart rate up to 1 hr following coronary occlusion. The means and standard deviation values for respiratory gas tensions obtained 1 day after infarction on 5 animals were P_{O_2} 71.3 $\pm$ 5.2 mm and P_{CO_2} 37.1 $\pm$ 3.6 mm, respectively. The preinfarct control values for P_{O_2} and P_{CO_2} were 76.1 $\pm$ 6.8 and 48.5 $\pm$ 6.2, respectively.

Discussion. The immediate findings following induced acute coronary occlusion were

TABLE I. Means and SD Values of Parameters Before and After Coronary Occlusion (18 dogs).

	Control	Postinfarct	
		Immediate[a]	Delayed[b]
Respiratory rate	11.3 ± 1.5	23.6 ± 4.0	25.0 ± 3.3
Heart rate	160.6 ± 6.7	156.2 ± 3.8	158.3 ± 3.5
$P_{a_{O_2}}$	74.0 ± 3.0	86.9 ± 3.3	78.9 ± 2.7
	40.8 ± 2.2	36.3 ± 1.1	37.0 ± 1.2
BP			
Systolic	173.0 ± 5.9	129.6 ± 9.8	133.5 ± 5.1
Diastolic	118.6 ± 4.9	87.5 ± 7.6	96.9 ± 4.0

[a] Up to 3 min.
[b] 10–60 min.

marked hyperpnea, systemic hypotension, reduction of arterial P_{CO_2}, and arterial hyperoxemia. We did not observe any significant changes in heart rate, even in the presence of marked systemic hypotension.

Hyperpnea following coronary occlusion has not previously been reported in experimental studies. It is however, interesting to note that dyspnea is the most common symptom in patients following acute myocardial infarction (1). The rapid onset of hyperpnea following acute coronary occlusion suggests a reflex phenomenon or an effect secondary to accompanying systemic hypotension. The hyperpnea occurred while the animal was under anesthesia and therefore it is improbable that it could be attributed to subjective pain. In one animal, the injection of 3 mg of microspheres intravenously did not cause any hyperpnea. Furthermore we were unable to find any microsphere in the lung tissue at gross and microscopic postmortem examination (9).

The marked hypotension was characterized by an immediate sharp decline in blood pressure lasting for approximately 2 min followed by a partial recovery. The hypotension may be due to either cardiogenic shock or shock secondary to hyperventilation or both. Progressive deterioration of cardiac function curves with rather stable systemic blood pressure and cardiac output has been reported with progressive injection of smaller sized microspheres in open-chest dogs (9).

The concomitant phenomena of hyperpnea and systemic hypotension were quite noticeable in almost all animals immediately after coronary embolization. It should be noted also that at the same time there was a fall in arterial CO_2 tension consistent with the hyperventilation. After this initial period, the respiration rate reached a plateau near its peak between 250 and 300% of control. Initially, the blood pressure response was a mirror image of the tachypneic response, showing a marked decline which was maximum after 30 sec after infarction. This was followed by a partial recovery and a plateau of the pressure response at around 60 to 70% of control, while the respiratory rate remained high.

Another noticeable finding was the increase of arterial P_{O_2} following coronary occlusion (sample obtained within 3 min after the procedure). There was also concomitant reduction of arterial P_{CO_2}. Our evidence, therefore, is quite different from the reported arterial hypoxemia with alveolar hyperventilation in clinical cases of unknown duration. The immediate arterial hyperoxemia could be explained partly due to hyperventilation and partly due to improvement of the altered V/Q ratio under anesthesia.

One day after infarction in the 5 animals studied, the hyperventilation was shown to persist as evidenced by reduction of arterial P_{CO_2}. There was also a trend toward arterial hypoxemia which could not be due to hypoventilation and must be due to other factors. It is possible that by the end of the first day after acute myocardial infarction, there are

pulmonary complications due to the left ventricular hemodynamic changes, which might interfere with gas exchange. Our findings of alveolar hyperventilation with possible arterial hypoxemia after 1 to 2 days following acute coronary occlusion would be consistent with the clinical data, although during the immediate postinfarction period arterial hyperoxemia exists. Postmortem studies in this series indicated gross pulmonary edema.

Summary. The immediate cardiopulmonary effects following acute induced coronary occlusion are hyperpnea, systemic hypotension, and hyperventilation. The onset of hyperpnea and systemic hypotension is quite rapid. Arterial blood gas tensions reveal arterial hyperoxemia and hypocapnia, which may be partly due to hyperventilation. Arterial hypoxemia, following myocardial infarction, is a later event and possibly related to the pulmonary complications following myocardial infarction.

1. Bean, W. E., Ann. Intern. Med. **11**, 2086 (1938).

2. Weil, M. H., and Shubin, H., Prog. Cardiovas. Dis. **11**, 1 (1958).

3. Valentine, P. A., Fhick, D. C., Mounsey, J. P. D., Reid, D., Shillingford, J. P., and Steiner, R. D., Lancet **2**, 837 (1966).

4. Shillingford, J. P., and Thomas, M., Amer. J. Cardiol. **20**, 484 (1967).

5. Sukumalchantra, Y., Danzig, R., Levy, S. D., and Swan, H. J. C., Circulation **41**, 641 (1970).

6. Cherniac, R. M., and Cuddy, R. E., Can. Med. Ass. J. **101**, 84 (1969).

7. Agress, C. M., Rosenberg, M. J., Binden, M. J., Schneiderman, A., and Clark, W. G., Amer. J. Physiol. **170**, 536 (1952).

8. DeBias, D. A., Birkhead, N. C., Banerjee, C., Kuroda, K., and Friedman, M. H. F., Fed. Proc., Fed. Amer. Soc. Exp. Biol. **29**, 3369 (1970).

9. Stone, H. L., Bishop, V. S., and Guyton, A. C., Amer. J. Physiol. **204**, 16 (1963).

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