Acute coronary insufficiency with normal coronary arteriograms

R. M. LAWSON
F.R.C.S.

S. RAHIMTOOLA
F.R.C.P.

J. ROSCH
M.D.

University of Oregon Medical School, 3181 S.W. Sam Jackson Park Road, Portland, Oregon 97201

Summary

Two patients presenting with apparent symptomatic and electrocardiographic evidence of acute coronary insufficiency and found to have normal coronary arteriograms are documented. The patients remain symptom free at follow-up 9 and 14 months later although one requires 160 mg propranolol daily. The electrocardiographic, myocardial metabolic and haemodynamic data in 413 patients with angina and normal coronary arteriograms are reviewed and the suggested aetiologies documented. Follow-up of patients in these series indicates a good prognosis for symptom-free survival.

Introduction

Although a normal coronary arteriogram may be seen in approximately 10% of patients undergoing coronary arteriography for angina pectoris (Kemp, Elliott and Gorlin, 1967; Kemp *et al.*, 1973) such a finding in the presence of acute coronary insufficiency (pre-infarction, accelerated angina) has been infrequently recorded. This report documents two such cases and briefly reviews the published findings in patients with angina and normal coronary arteriograms.

Case 1

A 53-year-old non-smoking, previously healthy woman presented with a 3½-year history of a squeezing, heavy substernal ache occasionally radiating to the right shoulder and arm and tending to occur with menstruation. The ache always rapidly cleared with glyceryl trinitrate. In the 3 weeks before admission, the pain had become much more frequent and severe, occurred at rest, awakened her from sleep, lasted up to 30 min at a time and was accompanied by nausea and dyspnoea.

On admission, her blood pressure was 150/85 mmHg; clinical examination of cardiovascular and

all other symptoms was unremarkable. Results of chest X-ray, haematology, electrolytes, blood urea, and serum enzymes (SGOT, LDH, SBD, and CPK) were all normal. ECG was normal with the patient pain-free, but showed 3 mm ST segment depression during attacks of pain (Fig. 1).

Coronary arteriograms performed for presumed coronary insufficiency were normal (Fig. 1). An exercise stress test performed during a pain-free period was markedly positive (ST depression 3 mm) but did not produce pain. Further investigations including cholecystogram, upper gastro-intestinal barium series and X-rays of cervical spine were also normal. Her pain again settled with glyceryl trinitrate and following reassurance she was discharged to the care of her internist. At follow-up at 9 months, the patient remained symptom free.

Case 2

A 56-year-old man was admitted with almost continual severe retrosternal pain radiating into the left arm of several hours' duration. Chest pain began 3 years earlier and steadily increased in severity and frequency. Two years before admission he was admitted to hospital for a presumed myocardial infarction, although this was not confirmed by ECG or enzyme studies. In the month before admission pain was noted on alternate days, came on with exertion but also at rest, lasted 5-15 min at a time, and was accompanied by dyspnoea. Medications before admission included thiazides for hypertension (2 years) and glyceryl trinitrate to which his chest pain usually responded.

Clinical examination revealed a blood pressure of 120/80 mmHg and a faint systolic murmur at the left sternal margin but was otherwise unremarkable. Results of chest X-ray, haematology, serum electrolytes, urea, enzymes (SGOT, LDH, SBD, CPK), glucose, cholesterol and triglycerides were normal. ECG showed marked ST depression during pain (Fig. 2) with return to a normal pattern after glyceryl trinitrate and analgesics. Coronary arteriograms

* Requests for reprints: Dr S. Rahimtoola, University of Oregon Medical School, 3181 S.W. Sam Jackson Park Road, Portland, Oregon 97201, U.S.A.

FIG. 1. A normal left coronary arteriogram. The right coronary arteriogram (not shown) was also normal. Marked ST depression is noted during pain.

FIG. 2. Normal right and left coronary arteriograms. Marked ST depression occurs with chest pain.

TABLE 1. Cardiac catheterization data (Case 2)

	Rest	Exercise	Valsalva	Amyl nitrate	Isoprenaline	Post-angiography
Pressures	LV 130/4	155/7	180/82	78/2 ⁺	115/10 ⁺	137/18
	BA 130/70	155/78	180/125	75/35	108/55	142/78
Cardiac output (resting)	5.1 l/min			End systolic volume index		17 ml/m ²
Cardiac index (resting)	2.8 l/min/m ²			Stroke volume index		53 ml/m ²
End diastolic volume index	70 ml/m ²			Ejection fraction		0.75

LV, left ventricle; BA, brachial artery; +, overshoot. All pressures simultaneous.

performed for presumed coronary insufficiency were normal (Fig. 2). He was reassured and discharged pain-free on glyceryl trinitrate and propranolol.

In the following 9 months he required two further admissions for recurrent severe chest pain. Further X-rays of cervical spine and barium studies of his upper gastro-intestinal tract were normal; acid stimulation of the distal oesophagus did not provoke pain. An echocardiogram showed asymmetrical septal hypertrophy but right and left heart catheterization revealed normal intracardiac pressures and no gradients at rest or after a Valsalva manoeuvre, amyl nitrate, isoprenaline, exercise, or angiography (Table 1). Left ventricular angiograms showed possible septal hypertrophy and normal LV wall motion, LV volumes, and ejection fraction. His ECG remained normal (when pain-free) but a stress ECG was markedly positive (ST depression of 2 mm) and produced pain.

He is currently, 14 months later, symptom-free and maintained on propranolol 160 mg/day and glyceryl trinitrate. Further tests have confirmed a prediabetic state.

Discussion

Elektrocardiographic, myocardial metabolic and haemodynamic data on 413 patients collected from nine published series of patients with angina and normal coronary arteriograms are illustrated in Table 2. Whereas angina pectoris secondary to coronary artery disease (CAD) is predominantly a male symptom, all series of patients with angina and normal coronary arteries (NCA) contain disproportionately large numbers of females and some contain females only. These patients are 10–15 years younger than their counterparts with CAD (Anderson *et al.*, 1972) and, although many have atypical angina (Kemp *et al.*, 1973; Boudoulas *et al.*, 1974; Bemiller, Pepine and Rogers, 1973; Waxler, Kimbiris and Dreifus, 1971), they frequently cannot be distinguished from patients with angina and CAD (Kemp *et al.*, 1973; Boudoulas *et al.*, 1974; Bemiller *et al.*, 1973; Waxler *et al.*, 1971; Dwyer, Wiener and Cox, 1969).

Hyperlipidaemia has been noted in from 8% (Waxler *et al.*, 1971) to 29% (Kemp *et al.*, 1973; Bemiller *et al.*, 1973; Dwyer *et al.*, 1969) of patients with NCA, and glucose intolerance in 14–43% (Kemp *et al.*, 1973; Bemiller *et al.*, 1973; Dwyer *et al.*, 1969; Likoff, Segal and Kasparian, 1967)—incidences approximately half of that seen in CAD (Kemp *et al.*, 1973). Smoking histories, when recorded, occurred in 41–80% of patients but did not significantly affect the ECG response to exercise (Waxler *et al.*, 1971). Family history was unhelpful (Dwyer *et al.*, 1969), no patient was anaemic and all had normal coronary arteriograms.

Abnormalities in the resting ECG were recorded in from 9% (Neill *et al.*, 1972) to 100% (Likoff *et al.*, 1967) of unselected patients. Patients with abnormal resting ECGs were deliberately excluded in one series (Arbogast and Bourassa, 1973).

Objective evidence of myocardial ischaemia has been sought in these patients in an attempt to explain their symptoms. Attention was focused on ECG changes following cardiac stimulation with exercise, hypoxaemia and/or pacing, changes in myocardial lactate metabolism after pacing or isoprenaline infusion, measurements of total and differential coronary flow, and myocardial oxygen uptake and cardiac haemodynamics at rest and after pacing or exercise. Findings have been compared with normal patients and/or with sex-age matched controls with angina and CAD (Bemiller *et al.*, 1973; Dwyer *et al.*, 1969; Neill *et al.*, 1972; Arbogast and Bourassa, 1973; Dwyer, Dell and Cannon, 1972; Eliot and Bratt, 1969). Differences in stimulating modes, rates of pacing and types and degrees of exercise must be remembered when assessing results.

Apparent ischaemic ECG changes have occurred in from 14% (Boudoulas *et al.*, 1974) to 100% (Likoff *et al.*, 1967; Neill *et al.*, 1972; Arbogast and Bourassa, 1973) of patients. However, pacing at over 170 beats/min did not produce any ST changes in twelve of twenty-nine patients in one series (Boudoulas *et al.*, 1974).

Myocardial lactate production or < 10% lactate extraction, as measured across the coronary bed, are

TABLE 2. Findings in 413 patients with angina and normal coronary arteriograms

Author	No.	Sex	Age	Abnormal resting ECG		Ischaemic ECG with exercise/hypoxia/pacing		Lactate abnormalities with pacing/isoprenaline		Coronary flow/myocardial O ₂ uptake	Cardiac haemodynamics
				No.	%	No.	%	No.	%		
Likoff <i>et al.</i> (1969)	15	F	15	30-52	15	100	15 (E)	100			Post-exercise pressures Normal in 8/8 Post-exercise LV angio-gram Normal in 6/6
Eliot <i>et al.</i> (1969)	15	F	15	18-38		15 (E and/or ECG)		100			Abnormal haemoglobin oxygen dissociation in 14/15 ↑ LVEDP } on exercise ↑ CI ↑ LVMWI
Dwyer <i>et al.</i> (1969)	10	F	6	34-52	6	60	2 (E)	20			Resting LVEDP > 12mm in 7/86
Waxler <i>et al.</i> (1971)	86	F	86	21-60	42	49	16/44 (E)	36			Normal blood O ₂ affinity in 10/10 LVEDP } Normal LV Volume } at rest LV Contractility }
Neill <i>et al.</i> (1972)	11	F	9	33-59	1	9	11($\frac{E}{H}$)	100	1/11 (P 120/min)	9	O ₂ uptake normal pre- and post-pacing in 11/11
Kemp <i>et al.</i> (1973)	200	F	99	19-68	103	51.5	31/152(E)	20	22/100 P 150/min, n=12 isoprenaline 2-6 mg/ml, n=88	22	Normal flow and O ₂ uptake in 18/18 at rest Normal flow in 6/6 & O ₂ uptake in 8/8 after isoprenaline
Bemiller <i>et al.</i> (1973)	37	F	16	26-62	20	51.5	27($\frac{E}{P}$)	73	10/14 (P)	71	↑ LVEDP } on exercise ↑ LVSWI } LVEDP/LVSWI abnormal at rest and on exercise
Arbogast and Bourassa (1973)	10	F	6	m 37	0	0	10(P)	100	5/10 (P 140/min)	50	↓ LVEDP } ↓ LVSWI } on pacing ↑ CI ↑ LVMWI
Boudoulas <i>et al.</i> (1974)	29	F	25-62	m 41	9	31	14(P) 4(E)	48 14	9/29 (P 170-180/min)	31	LV pressures, EF, EDV, contractility—normal pre-pacing EF, EDV not significantly changed after pacing

LVMWI, left ventricular work index; LVEDP, left ventricular end diastolic pressure; CI, cardiac index; LVSWI, left ventricular stroke work index; LVMWI, left ventricular minute work index; P, pacing; E, exercise; H, hypoxaemia; EF, ejection fraction; EDV, end diastolic volume.

indices of severe myocardial hypoxia (Shea *et al.*, 1962; Neill and Huckabee, 1966). Atrial pacing (Kemp *et al.*, 1973; Boudoulas *et al.*, 1974; Bemiller *et al.*, 1973; Neill *et al.*, 1972; Arbogast and Bourassa, 1973) or isoprenaline infusions (Kemp *et al.*, 1973) have shown such changes in 9–71% of cases. Pacing rates varied from 120 to 180/min but even at the latter rate, only nine of twenty-nine patients in Boudoulas' series produced lactate. Lactate production was two to three times more common in females (Kemp *et al.*, 1973; Bemiller *et al.*, 1973). Varying methodology in these series made assessment of lactate abnormalities concurrent with ischaemic ECG changes difficult. Only one of Neill's patients (paced at 120/min) produced lactate in the presence of an ischaemic ECG (Neill *et al.*, 1972), as did three of fourteen (Bemiller *et al.*, 1973) but nine of twenty-nine (paced at 180/min) did so (Boudoulas *et al.*, 1974). All patients in the latter series with > 2 mm ST depression produced lactate, whereas those with < 1 mm ST depression did not do so.

Correlation between the subjective sensation of angina, ischaemic ECG changes and lactate production was also difficult. None of Neill's patients complained of pain despite apparent ischaemic ECG changes in all and lactate production in one (Neill *et al.*, 1972); six of ten, all with ischaemic ECGs and five producing lactate (Arbogast and Bourassa, 1973) complained of pain, as did nine of fourteen lactate producers (two with ischaemic ECGs) (Bemiller *et al.*, 1973) and nine lactate producers all with ischaemic ECGs (Boudoulas *et al.*, 1974).

Myocardial oxygen uptake was normal at rest (Kemp *et al.*, 1973; Neill *et al.*, 1972) and after pacing (Neill *et al.*, 1972) and isoprenaline (Kemp *et al.*, 1973) in all patients examined. Coronary flow was also normal at rest and after isoprenaline when checked in six patients (Kemp *et al.*, 1973). Dwyer, using xenon 133 wash-out techniques, confirmed normal resting mean myocardial blood flows and further demonstrated normal resting mean regional flows in seven patients with angina and NCA (Dwyer *et al.*, 1972).

Left ventricular function (size, contractility and pressures) was normal at rest (Boudoulas *et al.*, 1974; Likoff *et al.*, 1967; Neill *et al.*, 1972) and after exercise (Likoff *et al.*, 1967). Left ventricular ejection fraction, end diastolic volume and contractility were unchanged after pacing; changes in end diastolic pressure were not considered reliable (Boudoulas *et al.*, 1974). Arbogast and Bourassa (1973) noted increases in cardiac index and left ventricular minute work index and falls in end diastolic pressure (LVEDP) and left ventricular stroke work index (LVSWI) after pacing at 140/min. Dwyer, using maximally tolerated work loads, also recorded increases in cardiac index and left ventricular work

index but noted an increase in LVEDP (Dwyer *et al.*, 1969).

Bemiller similarly showed increases in LVEDP on exercise accompanied by increases in LVSWI (Bemiller *et al.*, 1973). Left ventricular function as assessed by plotting LVEDP/LVSWI was abnormal at rest and on exercise, but less abnormal than sex-age matched controls with angina and CAD. Left ventricular function was unchanged and coronary arteriograms normal in seven patients when re-examined 4½ years later.

The aetiology remains enigmatic. Changes in coronary flow, apparently mediated by the vagus, have been produced in both anaesthetized and awake animals by gastric, oesophageal and common bile-duct distension (Gilbert, 1942; Cullen and Reese, 1952). ECG changes have been seen following gall-bladder manipulation at surgery and gross ST and T wave changes accompanied by severe retrosternal chest pain noted in a woman with marked oesophageal spasm (corkscrew oesophagus). Forrester, Herman and Gorlin (1970), however, noted no significant increase in the prevalence of gall-bladder disease, hiatus hernia, or cervical root disease in patients with angina and NCA when compared to normals. He concluded that these conditions were not major factors in the aetiology of the syndrome.

Misinterpretation of the coronary arteriograms is unlikely in the presence of widespread reports from excellent centres; the survival characteristics of these patients are not those of patients with CAD. Defects in haemoglobin oxygen dissociation noted in fourteen of fifteen young women (Eliot *et al.*, 1969) have not been confirmed by other workers (Kemp *et al.*, 1973; Neill *et al.*, 1972). Myocardial small vessel disease below the resolution of coronary arteriography is commonly associated with dysrhythmias, cardiomegaly and conduction disturbances (James, 1967), signs which were not especially common in the patients in these series. Furthermore, very few of these patients had conditions associated with small vessel disease. Dwyer *et al.* (1972) felt that their finding of normal regional myocardial blood flow tended to exclude small vessel disease or non-visualized atheroma, but Wells *et al.* (1967), noting conjunctival microcirculation abnormalities in eleven of twenty-seven patients with angina and NCA, thought that such abnormalities in the cardiac microcirculation might account for their symptoms. Although coronary artery spasm was not documented in these patients it cannot be excluded as an aetiological possibility and has been associated with variant angina pectoris (Kerin and Macleod, 1974).

Redistribution of blood within the myocardium (Zierler, 1967) in which total coronary flow and oxygen uptake might well remain normal, remains another possible explanation. Although normal

resting regional blood flow has been recorded (Dwyer *et al.*, 1972), similar studies during exercise or pacing have not yet, to the authors' knowledge, been performed in this group of patients.

The clinical presentation, laboratory findings, normal ventricular function (in contrast to that of sex-age matched controls with CAD) and follow-up data have led several workers to doubt the existence of myocardial ischaemia in these patients (Waxler *et al.*, 1971; Neill *et al.*, 1972; Arbogast and Bourassa, 1973). The significance of apparently ischaemic ECGs after pacing or exercise, and raised lactate levels in these anxious patients is questioned (Waxler *et al.*, 1971; Arbogast and Bourassa, 1973). Neill, Kassebaum and Judkins (1968) thought that myocardial hypoxia as shown by lactate production in one of their eleven patients, could reasonably explain that patient's symptoms. Although this patient did not suffer concurrent angina, a similar lack of temporal correlation between bouts of chest pain and chemical signs of myocardial hypoxia was noted in patients with angina and CAD (Neill, 1968).

Boudoulas *et al.* (1974) felt that the ability to elicit ECG and metabolic changes with pacing suggested that angina in some patients was related to myocardial ischaemia. The significance of their finding that patients paced at 180/min who had at least a 2 mm ST segment depression all secreted lactate is currently unknown. Although exercise produced angina and ECG changes more consistently in their control group with CAD, Dwyer *et al.* (1969) noted clinical and haemodynamic abnormalities in both groups which were not significantly different.

Bemiller *et al.* (1973), although finding evidence of abnormal ventricular function in their patients, were sufficiently impressed by the lack of deterioration in ventricular function and coronary arteriograms over 4½ years to suggest a non-progressive disorder.

Although lactate abnormalities and ECG changes seen in many of these patients make a purely functional aetiology unlikely, much of circulatory control and cellular metabolism remains unknown; the disproportionately high female incidence with implied tissue hormonal changes may be significant. Several of the suggested aetiological factors may together be relevant (Kemp *et al.*, 1973).

Normal coronary arteriograms were noted in 19% of a series of seventy-nine patients with acute coronary insufficiency (Scanlon *et al.*, 1973). Both the patients in the present report historically, clinically, and electrocardiographically appeared to present with acute coronary insufficiency. In the presence of normal coronary arteriograms other aetiological possibilities had to be excluded. Although these tests were negative, the dynamic nature of the symp-

toms suggest that repetition of some examinations during pain might be of interest. The significance of asymmetrical septal hypertrophy in the presence of a normal clinical examination, ECG, LVEDP, and absent outflow gradient is uncertain. Further follow-up may clarify this finding.

Whatever the aetiology, the prognosis appears good for these patients. In 864 patient years of follow-up, seven deaths occurred (Kemp *et al.*, 1973; Bemiller *et al.*, 1973; Waxler *et al.*, 1971; Neill *et al.*, 1972) an annual mortality (0.81%) much below the 2.9% recorded in non-operated patients with at least 50% stenosis in a single coronary artery (Bruschke, Proudfit and Sones, 1973). Survival is no different from that of the general population (Kemp *et al.*, 1973).

Post-mortem examinations in two of the seven deaths revealed normal hearts and no explanation for demise. The cause of death was unknown in three and non-cardiac in the remaining two. Dwyer *et al.* (1969) also recorded a sudden death in a young man; a normal heart was found at post-mortem and no cause of death was found.

Eliot *et al.* (1969) noted sub-endocardial infarctions in the presence of normal coronary arteries and histologically normal small vessels in all three young women dying within a few months of coronary arteriography. The significance of haemoglobin oxygen dissociation abnormalities in their patients remains uncertain. Whether these patients represent a subgroup with a peculiarly critical sub-endocardial oxygen supply/demand balance remains unknown. Symptomatically, 45–80% (Kemp *et al.*, 1973; Bemiller *et al.*, 1973; Waxler *et al.*, 1971; Neill *et al.*, 1972) of patients had a reduction in chest pain, often without therapy. Only 6–19% (Kemp *et al.*, 1973; Waxler *et al.*, 1971; Neill *et al.*, 1972) noted worsening of symptoms and these usually responded to nitrates and/or propranolol, psychotherapy being of very limited value (Kemp *et al.*, 1973).

Conclusions

Angina occurring in the presence of normal coronary arteriograms is predominantly a symptom of women in the age range of 35–45 years. Myocardial oxygen uptake and total coronary flow was normal at rest and after stimulation (pacing/isoprenaline), in all tested patients and regional coronary flow was normal at rest. Varying lactate production occurred and was difficult to correlate with angina and ischaemic ECG changes. Changes in left ventricular function on stimulation depended on the stimulating mode. Abnormalities of LV function on exercise testing in one series were less marked than in sex-age matched controls with coronary artery disease, and were unchanged 4½ years later. Although the aetiology remains uncertain, several workers doubt the

existence of myocardial ischaemia in these patients, whereas others feel that a functional aetiology is unlikely.

Several factors, and perhaps others hitherto unknown, may be relevant. Survival for these patients is no different from that of the general population.

References

- ANDERSON, R.P., HODAM, R., WOOD, J. & STARR, A. (1972) Direct revascularization of the heart. Early clinical experience with 200 patients. *Journal of Thoracic and Cardiovascular Surgery*, **63**, 355.
- ARBOGAST, R. & BOURASSA, M.G. (1973) Myocardial function during atrial pacing in patients with angina pectoris and normal coronary arteriograms. *American Journal of Cardiology*, **32**, 257.
- BEMILLER, C.R., PEPINE, C.J. & ROGERS, A.K. (1973) Long-term observations in patients with angina and normal coronary arteriograms. *Circulation*, **42**, 36.
- BOUDOULAS, H., COBB, T.C., LEIGHTON, R.F. & WILT, S.M. (1974) Myocardial lactate production in patients with angina-like chest pain and angiographically normal coronary arteries and left ventricle. *American Journal of Cardiology*, **34**, 501.
- BRUSCHKE, A.V.G., PROUDFIT, W.L. & SONES, F.M. (1973) Progress study of 590 consecutive nonsurgical cases of coronary disease followed by 5-9 years. *Circulation*, **42**, 1147.
- CULLEN, M.L. & REESE, H.L. (1952) Myocardial circulatory changes measured by clearance of Na_{24} —effect of common duct distension on myocardial circulation. *Journal of Applied Physiology*, **5**, 281.
- DWYER, E.M., DELL, R.B. & CANNON, B.J. (1972) Regional myocardial blood flow in patients with angina and normal coronary arteries. *Circulation*, **46** (Suppl. 11), 11.
- DWYER, E.M., WIENER, L. & COX, J.W. (1969) Angina pectoris in patients with normal and abnormal coronary arteriograms. *American Journal of Cardiology*, **23**, 639.
- ELIOT, R.S. & BRATT, G. (1969) The paradox of myocardial ischemia and necrosis in young women with normal coronary arteriograms. Relation to abnormal hemoglobin-oxygen dissociation. *American Journal of Cardiology*, **23**, 633.
- FORRESTER, J.S., HERMAN, M.V. & GORLIN, R. (1970) Non-coronary factors in the anginal syndrome. *New England Journal of Medicine*, **283**, 786.
- GILBERT, N.D. (1942) Influence of intrinsic factors on the coronary flow and clinical course of heart disease. *Bulletin of the New York Academy of Medicine*, **18**, 83.
- JAMES, T.N. (1967) Pathology of small coronary arteries. *American Journal of Cardiology*, **20**, 679.
- KEMP, H.G., ELLIOTT, W.C. & GORLIN, R. (1967) The anginal syndrome with normal coronary arteriography. *Transactions of the Association of American Physicians*, **80**, 59.
- KEMP, H.G., VOKONAS, P.S., COHN, P.F. & GORLIN, R. (1973) The anginal syndrome associated with normal coronary arteriograms. *American Journal of Medicine*, **54**, 735.
- KERIN, N. & MACLEOD, C. (1974) Coronary artery spasm associated with variant angina pectoris. *British Heart Journal*, **36**, 224.
- LIKOFF, W., SEGAL, B.L. & KASPARIAN, H. (1967) Paradox of normal selective coronary arteriograms in patients considered to have unmistakable coronary heart disease. *New England Journal of Medicine*, **276**, 1063.
- NEILL, W.A. (1968) Myocardial hypoxia and anaerobic metabolism in coronary heart disease. *American Journal of Cardiology*, **22**, 507.
- NEILL, W.A. & HUCKABEE, W.E. (1966) Anaerobic heat production by the heart. *Journal of Clinical Investigation*, **45**, 1412.
- NEILL, W.A., JUDKINS, M.P., DHINSA, D.S., METCALFE, J., KASSEBAUM, D.G. & KLOSTER, F.E. (1972) Clinically suspect ischemic heart disease not corroborated by demonstrable coronary artery disease. *American Journal of Cardiology*, **29**, 171.
- NEILL, W.A., KASSEBAUM, D.G. & JUDKINS, M.P. (1968) Myocardial hypoxia as the basis for angina pectoris in a patient with normal coronary arteriograms. *New England Journal of Medicine*, **279**, 789.
- SCANLON, P.J., NEMICKAS, R., MORAN, J.F., TALANO, J.R., AMIRPARVIZ, F. & PIFARRE, R. (1973) Accelerated angina pectoris. Clinical, hemodynamic, arteriographic, and therapeutic experience in 85 patients. *Circulation*, **47**, 19.
- SHEA, T.M., WATSON, R.M., PIOTROWSKI, F., DERMKSAN, G. & CASE, R.B. (1962) Anaerobic myocardial metabolism. *American Journal of Physiology*, **203**, 463.
- WAXLER, E.B., KIMBIKIS, D. & DREIFUS, L.S. (1971) The fate of women with normal coronary arteriograms and chest pain resembling angina pectoris. *American Journal of Cardiology*, **28**, 35.
- WELLS, R., HEINLE, R.A., KEMP, H.G., GORLIN, R. & HERMAN, M.V. (1967) Abnormalities of the microcirculation in patients with anginal syndrome with normal coronary arteries studied by cineangiography. *Circulation*, **36** (Suppl. 11), 11.
- ZIERLER, K. (1967) In discussion of: KEMP, H.G., ELLIOTT, W.C. & GORLIN, R. The anginal syndrome with normal coronary arteriography. *Transactions of the Association of American Physicians*, **80**, 59.