method used were important elements of later, more generally successful methods (Conant *et al.*, 1968).

This paper is a report to the Public Health Laboratory Service Working Party on Epidemic Non-bacterial Gastroenteritis.

We wish to thank Dr. T. A. A. Hunter, Medical Officer, Marlborough College, for his invaluable work in documentation of the principal epidemic described and the collection of specimens. We should also like to thank the volunteers for their willing help, Miss J. M. Bailey, S.R.N., for nursing assistance, and numerous other colleagues for help in the laboratory work.

Some of this work was supported by a grant from the Department of Health and Social Security.

Requests for reprints should be sent to: Dr. S. K. R. Clarke, Public Health Laboratory, Kingsdown, Bristol BS2 8EL.

References

Adler, J. L., and Zickl, R. (1969). *Journal of Infectious Diseases*, **119**, 668.
Bradley, W. H. (1943). *British Medical Journal*, **1**, 309.
Conant, R. M., Hamparian, V. V., Stott, E. J., and Tyrrell, D. A. J. (1968). *Nature*, **217**, 1264.
Dolin, R., *et al.* (1971). *Journal of Infectious Diseases*, **123**, 307.
Egglestone, S. I. (1968). Ph.D. Thesis, University of Bristol.
Gordon, I., Ingraham, H. S., and Korns, R. F. (1947). *Journal of Experimental Medicine*, **86**, 409.
Gray, J. D. (1939). *British Medical Journal*, **1**, 209.
Jordan, W. S., Gordon, I., and Dorrance, W. R. (1953). *Journal of Experimental Medicine*, **98**, 461.
Reimann, H. A., Price, A. H., and Hodges, J. H. (1945). *Proceedings of the Society for Experimental Biology and Medicine*, **59**, 8.
Rubenstein, D., and Tyrrell, D. A. J. (1970). *British Journal of Experimental Pathology*, **51**, 210.
Zahorsky, J. (1929). *Archives of Pediatrics*, **46**, 391.

PRELIMINARY COMMUNICATIONS

Autonomic Disturbance at Onset of Acute Myocardial Infarction

S. W. WEBB, A. A. J. ADGEY, J. F. PANTRIDGE

British Medical Journal, 1972, 3, 89–92

Summary

Of 74 patients seen within 30 minutes of the onset of acute myocardial infarction 68 (92%) had signs of autonomic imbalance. Excessive vagal activity was evident in 41 (55%) and there was sympathetic overactivity in 27 (36%). The high incidence of sudden death in the acute phase of a coronary attack probably results from the electrical imbalance caused by autonomic disturbance. This disturbance must therefore be taken into account in any prophylactic regimen against the lethal early ventricular dysrhythmias.

Introduction

Most deaths from acute myocardial infarction occur within one hour of the onset of symptoms (Fulton *et al.*, 1969), and the median of the period between onset and admission to hospital is more than eight hours (McNeilly and Pemberton, 1968). Attention has therefore been directed to the prehospital phase of the acute coronary attack (Pantridge and Geddes, 1966, 1967). Ventricular fibrillation occurs most often immediately after the onset of acute myocardial infarction and is the cause of most deaths (Pantridge and Geddes, 1967; Pantridge and Adgey, 1969). Understanding the factors that initiate ventricular fibrillation may enable us to prevent it.

Self-injection of atropine and lignocaine has been advocated as a way of reducing the prehospital mortality in coronary attacks (Levine, 1969; Sarnoff, 1970; Friedberg, 1972; Yu, 1972). It therefore seems important to know the incidence of autonomic disturbance and to assess the effects of these drugs in treating it. We have recorded data on 558 patients seen within one hour of the onset of acute infarction and in most cases managed by a mobile coronary care unit. The last 200 of them were studied by a continuous recording of the cardiogram and frequent recordings of the blood pressure. The observer, usually one of us (S.W.W.), was confident that in 88 of these 200 patients the interval between the onset of symptoms and the start of observation was less than 30 minutes.

This communication deals with these 88 patients (81 men and 7 women), all of whom fulfilled the criteria for indubitable infarction previously described (Adgey *et al.*, 1968; Adgey *et al.*, 1971).

Cardiac Department, Royal Victoria Hospital, Belfast
S. W. WEBB, B.SC., M.R.C.P., Research Fellow
A. A. J. ADGEY, M.R.C.P., Physician
J. F. PANTRIDGE, M.D., F.R.C.P., Physician-in-charge

Patients

The mean age of the 81 men was 56 years and that of the seven women 63 years. Forty-two patients had anterior infarction, 44 posterior infarction, and two anterior subendocardial infarction. Thirty-four (39%) had had a previous infarct. Thirteen (15%) had ventricular fibrillation when first seen and were therefore excluded from the study of autonomic disturbance. Another patient was excluded because of the possibility of previous hypertension.

In the remaining 74 patients the heart rate and rhythm and the blood pressure were observed immediately the patient was seen and before analgesic or other therapy. None of the patients had been taking beta-blocking drugs, digitalis, or hypotensive agents.

Patients with sinus tachycardia (heart rate of 100 or more) with or without transient hypertension were considered to show sympathetic overactivity. Transient hypertension (blood pressure of 160/100 mm Hg or higher) in the absence of sinus tachycardia was also regarded as evidence of sympathetic overactivity, since a reflex sympathetic pressor response with minimal alteration in the heart rate has been described (Malliani *et al.*, 1969; Peterson and Brown, 1971). Patients who had sinus bradycardia (heart rate of 60 or less) or atrioventricular block (second-degree or complete) were considered to show parasympathetic overactivity, as also were those with transient hypotension (systolic blood pressure 100 mm Hg or lower) in the absence of pronounced bradycardia.

Incidence of Autonomic Disturbance

The incidence of autonomic disturbance at the initial observation is shown in Fig. 1. Only six patients (8%) had a normal heart rate and normal blood pressure. Twenty-seven patients (36%) showed evidence of sympathetic overactivity. Seventeen of them had sinus tachycardia, accompanied in nine by hypertension, and 10 had transient hypertension with a heart rate in the normal range.

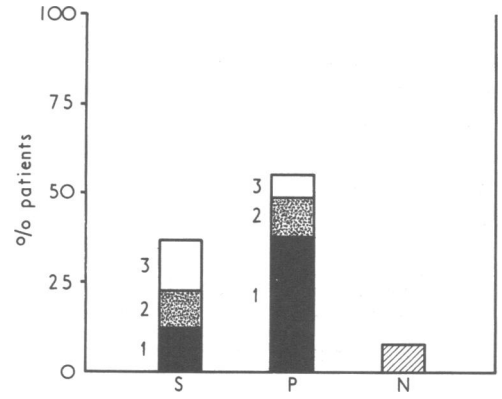

FIG. 1—Evidence of autonomic disturbance in 74 patients seen within 30 minutes of onset of symptoms. S = Sympathetic overactivity. P = Parasympathetic overactivity. N = Normal heart rate and blood pressure. S1 = Sinus tachycardia with hypertension. S2 = Sinus tachycardia. S3 = Transient hypertension. P1 = Bradyarrhythmia with hypotension. P2 = Bradyarrhythmia. P3 = Transient hypotension.

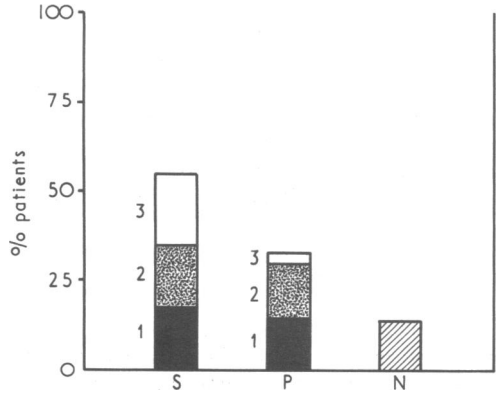

FIG. 2—Evidence of autonomic disturbance in 35 patients with anterior infarction seen within 30 minutes. Key as for Fig. 1.

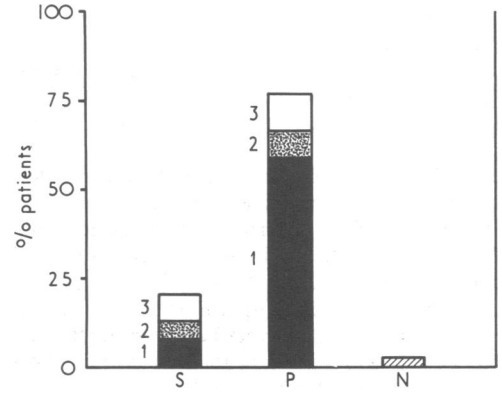

FIG. 3—Evidence of autonomic disturbance in 39 patients with posterior infarction seen within 30 minutes. Key as for Fig. 1.

Parasympathetic overactivity was present in 41 patients (55%). Thirty-six of them had bradyarrhythmia and 28 of these had associated hypotension. Nineteen of the 28 with bradyarrhythmia and hypotension had a systolic blood pressure of 80 mm Hg or lower. Eight patients had complete atrioventricular block, and in all of them the systolic blood pressure was 80 mm Hg or lower. In five patients transient hypotension (range 0-90 mm Hg) occurred in the presence of a normal heart rate and normal atrioventricular conduction.

The incidence of autonomic disturbance in the 35 patients with anterior infarction is shown in Fig. 2. Sympathetic overactivity was observed in 19 (54%) and parasympathetic overactivity in 11 (32%). Five of the 35 had a normal heart rate and normal blood pressure.

The incidence of autonomic disturbance in the 39 patients with posterior infarction is shown in Fig. 3. Eight patients (20%) showed sympathetic overactivity, while 30 (77%) had parasympathetic overaction. One patient had a normal heart rate and normal blood pressure. Evidence of parasympathetic overactivity was invariably present in patients with posterior infarction who had not had a previous infarction, which might have interfered with vagal receptors.

Management

Immediately their heart rate and rhythm and blood pressure had been recorded all patients were given 5·0 mg of diamorphine intravenously. Many needed a further 5·0 mg to relieve pain. In four of the five patients with hypotension in the presence of a normal heart rate the blood pressure rose to normal when their pain was relieved.

Twenty of the 28 patients with bradyarrhythmia and hypotension required atropine (see Table). Eight of the 20 had complete heart block. Eleven of 12 with sinus bradycardia and hypotension had a prompt rise in heart rate and blood pressure. The mean heart rate rose from 55 to 93 and the mean systolic blood pressure from 84 to 129 mm Hg. The dose of atropine ranged from 0·3-1·2 mg (mean 0·75 mg). Atropine was administered carefully intravenously in aliquots of 0·3 or 0·6 mg. In four patients, despite careful titration of the dosage, the heart rate after atropine exceeded 100.

The amount of atropine given to the eight patients with atrioventricular block ranged from 0·6-2·4 mg (mean 1·3 mg). Improvement in conduction occurred promptly in five of the patients and the blood pressure rose to normal levels with the rise in ventricular rate. Sinus rhythm was established in all five and ventricular pacing was not required. Severe tachycardia occurred in two patients when normal atrioventricular conduction was established. The blood pressure failed to rise in one patient when atrioventricular block was corrected. Atropine did not influence conduction in the remaining two patients with complete block. In one of them normal atrioventricular conduction was resumed after two hours of ventricular pacing, so in this case the atropine dosage may have been inadequate. The dose of 0·6 mg given to the other patient was certainly inadequate.

Thus 20 (27%) of the patients studied required atropine for bradyarrhythmia and associated hypotension. A rise in heart

Effect of Atropine in Patients with Bradyarrhythmia and Hypotension

	No. of Patients	No. with Hypotension	No. given Atropine for Bradyarrhythmia with Hypotension	Effect		
				Rise in Heart Rate and Blood Pressure	Rise in Heart Rate	None
Sinus bradycardia	28	20	12	11 (4)	1	0
Complete heart block	8	8	8	5 (2)	1 (1)	2
Total	36	28	20	16 (6)	2 (1)	2

Figures in parentheses indicate patients who developed a heart rate over 100/min.

rate and blood pressure was observed in 16 of the 20. However, despite careful titration of the atropine dosage a heart rate exceeding 100/min occurred in 6 of the 16.

The effect of intravenous practolol was investigated in patients who presented with sinus tachycardia or sinus tachycardia combined with hypertension. Its effect on sinus tachycardia which appeared on correction of vagal overactivity was also assessed. The effect of practolol on sinus tachycardia in a normotensive patient is shown in Fig. 4. Heart rate was reduced from 125 to 100, the blood pressure was unaltered, and the S-T segment elevation was reduced. The fall in S-T segment which accompanied the fall in the heart rate is regarded as evidence of reduction in the severity of the myocardial ischaemic injury (Maroko *et al.*, 1971). The control by practolol of the sympathetic overactivity unmasked by atropine given for the correction of atrioventricular block is shown in Fig. 5.

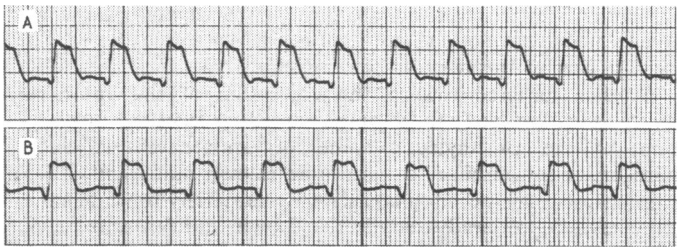

FIG. 4—Effect of practolol in a normotensive patient with sinus tachycardia. A, Sinus tachycardia (rate 125); S-T rise 6·5 mm. B, Five minutes after practolol 10 mg intravenously; rate 100; S-T rise 5·0 mm.

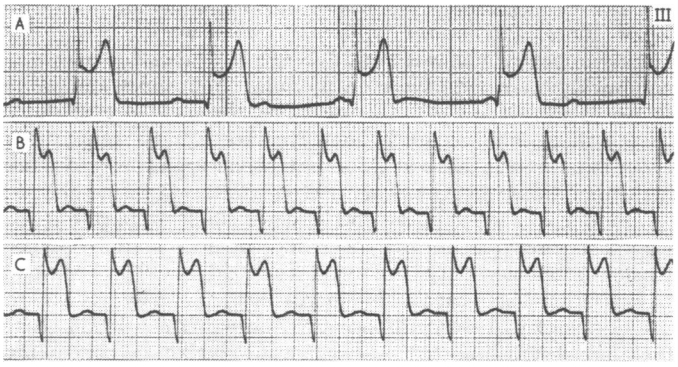

FIG. 5—Effect of practolol on sinus tachycardia after correction of complete heart block by atropine. A, Complete heart block in patient with posterior infarct; ventricular rate 48/min. B, Sinus tachycardia (rate 120) persisting three hours after atropine 2·0 mg; S-T segment 11·5 mm. C, Five minutes after practolol 20 mg intravenously given in aliquots of 5 mg; rate 100; S-T rise 9·0 mm.

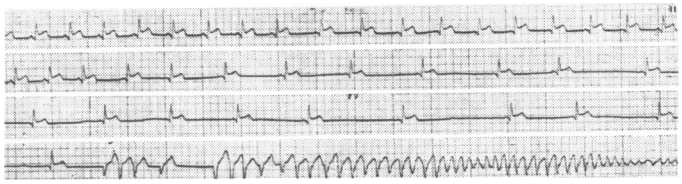

FIG. 6—Ventricular fibrillation precipitated by bradycardia. Acute posterior infarct (continuous record lead II in patient's home). Sudden vagal discharge leads to bradycardia and ventricular fibrillation.

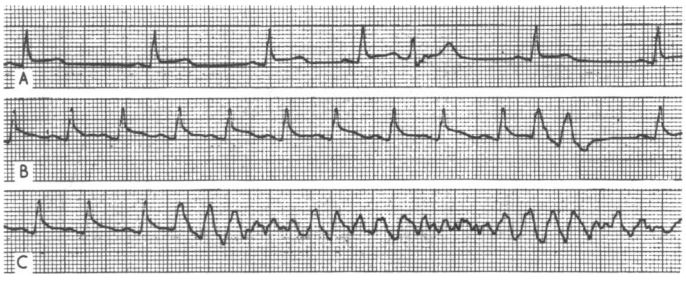

FIG. 7—Sinus tachycardia after atropine, leading to ventricular fibrillation. Patient with anterior infarction lead I. A, Sinus bradycardia (rate 55) with ventricular ectopics. B, Two minutes after atropine 0·6 mg intravenously, sinus tachycardia (rate 110) with consecutive ventricular ectopics. C, Three minutes after atropine, development of ventricular fibrillation.

Discussion

These observations are relevant to sudden death in acute myocardial infarction. Sympathetic and parasympathetic overactivity may each be related to the development of ventricular fibrillation.

A sympathetic reflex excited by experimental coronary occlusion has been described (Malliani *et al.*, 1969), and stimulation of the cardiac sympathetic nerves gives rise to increased temporal dispersion of the recovery of excitability and lowers the ventricular fibrillation threshold (Han and Moe, 1964; Han *et al.*, 1964). Sympathetic denervation and beta-receptor blocking agents will suppress the ventricular dysrhythmia produced by experimental coronary occlusion (Ebert *et al.*, 1967; Ceremuzynski *et al.*, 1969).

Sympathetic overactivity at the initial examination occurred in 27 (36%) of the 74 patients. In addition sympathetic overactivity was unmasked by atropine in seven who initially showed clinical evidence of vagal overactivity. Thus evidence of sympathetic overactivity was obtained in 34 patients (46%). However, vagal overactivity has been more often implicated in sudden death (Richter, 1959). The existence of a cardiogenic reflex resulting in a combination of arterial hypotension and bradycardia has long been recognized (von Bezold, 1867).

At slow heart rates there is an increase in the temporal dispersion of recovery and therefore a fall in the ventricular fibrillation threshold (Han *et al.*, 1966). In the acute phase of myocardial infarction vagal discharge may be abrupt and intense (Fig. 6). The incidence of vagal overactivity among patients in this study was high. It occurred in 29 (63%) of those with a first infarct. When this was a posterior infarct vagal overactivity was invariable.

Early complete atrioventricular block complicating acute infarction often results from vagal discharge and therefore responds to atropine (Adgey *et al.*, 1968). In three-quarters of the present patients with complete atrioventricular block seen within the first 30 minutes normal conduction was resumed after atropine, and ventricular pacing was not required.

SELF-ADMINISTRATION OF ATROPINE

The data presented here suggest that in most patients, perhaps in all, autonomic disturbance occurs immediately after the onset of infarction. Supporters of the importance of vagal overactivity have advocated the self-administration of atropine by intramuscular injection (Levine, 1969; Sarnoff, 1970; Friedberg, 1972; Yu, 1972), and it has been suggested that high-risk coronary patients might always carry an automatic injector containing 2 mg of atropine. A simple photoelectric fingerstall device should enable their heart rate and rhythm to be transmitted by telephone to their doctor. If the heart rate were less than 60 the patient would be instructed to give himself atropine.

However, while the two divisions of the autonomic system exert antagonistic effects the opposing influences are not algebraically additive. The cardiac acceleration produced by strong sympathetic stimuli is usually overpowered by even relatively weak vagal activity (Samaan, 1935). A similar negative sympathetic parasympathetic interaction has also been observed in relation to the regulation of myocardial contractility (Levy and Zieske, 1969). The correction of mild or moderate vagal overactivity may unmask severe sympathetic overactivity and precipi-

tate ventricular fibrillation (Fig. 7). In this study 7 (35%) of the 20 patients who required atropine for bradyarrhythmia and hypotension developed an inappropriately rapid heart rate, despite careful titration of the dosage.

Studies directed toward the correction of the autonomic disturbance are likely to be more rewarding than the investigation of the prophylactic value of antiarrhythmic agents with an action similar to lignocaine (Lown and Wolf, 1971). Lignocaine may be an unsatisfactory antiarrhythmic agent in the presence of bradyarrhythmia (Lown and Vassaux, 1968; Han, 1969). There is also evidence that it is unsatisfactory in the presence of tachycardia (Geddes *et al.*, 1972).

Among patients who survive the risk of sudden death autonomic disturbance may be important in relation to the size of the area of infarction and therefore to the incidence of cardiogenic shock and pump failure. Patients who come under intensive care early in whom bradycardia and other dysrhythmias are quickly corrected have a low mortality from shock and pump failure (Pantridge, 1970). Furthermore, the incidence of shock among those who get early intensive care is very significantly lower than among those in whom intensive care is delayed more than three hours (Adgey *et al.*, 1971).

There has been clinical and experimental support for the view that the area of infarction may be increased by hypotension after coronary occlusion (Pantridge, 1970; Maroko *et al.*, 1971). Tachycardia also increases the severity and extent of the myocardial ischaemic injury (Maroko *et al.*, 1971). It is therefore interesting that practolol was valuable in controlling the manifestations of sympathetic overactivity which occurred in 46% of patients in this study.

Conclusion

The data presented here show that trying to correct autonomic disturbance after acute myocardial infarction is rewarding. Seventy-two of the 74 patients were aged under 70 and 65 of them survived the three-week period in hospital—an overall mortality of 9·7%. A mortality of more than 26% might have been expected since 30 of 117 patients in the Bristol study who sought medical help within one hour died (Mather *et al.*, 1971), and it is known that most deaths in the first hour occur within the first 30 minutes (McNeilly and Pemberton, 1968).

References

Adgey, A. A. J., Geddes, J. S., Mulholland, H. C., Keegan, D. A. J., and Pantridge, J. F. (1968). *Lancet*, **2**, 1097.
Adgey, A. A. J., *et al.* (1971). *Lancet*, **2**, 501.
Bezold, A. von. (1867). *Untersuchungen Physiologisches Laboratorium zu Wurzburg*, **1**, 95.
Ceremuzynski, L., Staszewsaka-Barczak, J., and Herbaczynska-Cedro, K. (1969). *Cardiovascular Research*, **3**, 190.
Ebert, P. A., Allgood, R. J., and Sabiston, D. C. (1967). *Surgical Forum*, **18**, 114.
Friedberg, C. K. (1972). *Circulation*, **45**, 179.
Fulton, M., Julian, D. G., and Oliver, M. F. (1969). *Circulation*, **40**, Suppl. No. 4, p. 182.
Geddes, J. S., Webb, S. W., and Pantridge, J. F. (1972). Unpublished.
Han, J. (1969). *American Journal of Cardiology*, **24**, 800.
Han, J., and Moe, G. K. (1964). *Circulation Research*, **14**, 44.
Han, J., de Jalon, P. G., and Moe, G. K. (1964). *Circulation Research*, **14**, 516.
Han, J., Millet, D., Chizzonitti, B., and Moe, G. K. (1966). *American Heart Journal*, **71**, 481.
Levine, H. J. (1969). *American Journal of Cardiology*, **24**, 826.
Levy, M. N., and Zieske, H. (1969). *Journal of Applied Physiology*, **27**, 465.
Lown, B., and Vassaux, C. (1968). *American Heart Journal*, **76**, 586.
Lown, B., and Wolf, M. (1971). *Circulation*, **44**, 130.
McNeilly, R. H., and Pemberton, J. (1968). *British Medical Journal*, **3**, 139.
Malliani, A., Schwartz, P. J., and Zanchetti, A. (1969). *American Journal of Physiology*, **217**, 703.
Maroko, P. R., *et al.* (1971). *Circulation*, **43**, 67.
Mather, H. G., *et al.* (1971). *British Medical Journal*, **3**, 334.
Pantridge, J. F. (1970). *Quarterly Journal of Medicine*, **39**, 621.
Pantridge, J. F., and Adgey, A. A. J. (1969). *American Journal of Cardiology*, **24**, 666.
Pantridge, J. F., and Geddes, J. S. (1966). *Lancet*, **1**, 807.
Pantridge, J. F., and Geddes, J. S. (1967). *Lancet*, **2**, 271.
Peterson, D. F., and Brown, A. M. (1971). *Circulation Research*, **28**, 605.
Richter, C. P. (1959). In *The Meaning of Death*, ed. H. Feifel, chapt. 18. New York, McGraw-Hill.
Samaan, A. (1935). *Journal of Physiology*, **83**, 332.
Sarnoff, S. J. (1970). Carl J. Wiggers Award Lecture, American Physiological Society.
Yu, P. N. (1972). *Circulation*, **45**, 189.

MEDICAL MEMORANDA

Treatment of Bacterial Endocarditis: Complicating Haemodialysis

LEOPOLDO F. SALDANHA, RALPH GOLDMAN, KENNETH ADASHEK, DONALD G. MULDER

British Medical Journal, 1972, **3**, 92–93

Several reports (Brescia *et al.*, 1966; Goodman *et al.*, 1969; Kurtz, 1969; Ribot *et al.*, 1971; Ribot and Frankel, 1971) have brought attention to the occurrence of bacterial endocarditis as a complication of chronic haemodialysis. We report an additional case of acute aortic insufficiency secondary to *Staphylococcus aureus* bacterial endocarditis treated successfully with antibiotics and emergency aortic valve replacement. The most probable source of infection was the arteriovenous Teflon-Silastic shunt.

University of California, Los Angeles, School of Medicine, Los Angeles, California 90024, U.S.A.
LEOPOLDO F. SALDANHA, M.D., Fellow in Nephrology
RALPH GOLDMAN, M.D., Professor of Medicine
KENNETH ADASHEK, M.D., Resident in Medicine (Present address: U.S.P.H.S., San Diego, California)
DONALD G. MULDER, M.D., Professor of Surgery

Case Report

The patient was a 33-year-old man in whom a diagnosis of lupus nephritis had been made in 1967. Despite treatment with prednisone, he became progressively uraemic, and haemodialysis was initiated in July 1968.

The arteriovenous shunt was relatively free of complications until December 1970, when surgical revisions were necessary because of poor blood flow and infection. Fever developed and antibiotic treatment was initiated. He had anorexia, orthopnoea, paroxysmal nocturnal dyspnoea, and chest "heaviness" when recumbent for two weeks before admission. On the day of admission he awakened with sudden severe substernal pain. When seen he was in acute respiratory distress. The blood pressure was 140/60, the pulse 90/min. and irregular, and the temperature 40·5°C. There were inspiratory rales in the lung bases. On auscultation a gallop rhythm and a systolic ejection murmur at the aortic area were heard, radiating along the left sternal border and