

Cardiac disease accompanying allergic drug reactions

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It has been known for many years that the heart can be the target organ of an allergic response.¹⁻⁵ Feigen and associates⁶ have shown that sensitized guinea pig heart may respond to an antigen, such as ovalbumin, with decrease in coronary flow and atrial fibrillation. Histamine was isolated in the perfusate and was probably responsible for the acceleration of the heart rate and a decrease in coronary flow. The most intense effect was atrial fibrillation. These effects could be reproduced by an appropriate dose of histamine.

Electrocardiographic abnormalities during anaphylaxis in guinea pigs, dogs, and rabbits have included arrhythmias, significant depressions in the S-T segments, and changes in the QRS and T waves.^{7, 10} Patterson and colleagues^{15, 16} studied anaphylaxis in monkeys with human sera. They demonstrated post-mortem cardiac abnormalities after anaphylactic shock in all the animals tested. Arteritis, focal necrosis, and inflammatory cells were present in the myocardium. Changes were noted by electron microscopy in the nature of increase in sarcoplasm or cytoplasmic ground substance.

Harkavy¹¹ summarized 32 cases, including his own and those found in the literature, of cardiac involvement due to allergy. Two patients sustained a myocardial infarction and 13 patients manifested arrhythmias. McManus and Lawlor¹² reported a case of myocardial infarction following the administration of tetanus antitoxin and cited 3 others from the literature.

Binder and associates¹³ reported 3 patients who developed severe allergic reactions during the course of penicillin therapy and whose electrocardiograms showed transient changes. It is significant that 2 of the 3 patients were under the age of 30. All had skin and joint changes associated with findings suggestive of cardiac disease. Twenty-five additional patients with mild allergic reactions due to penicillin had normal electrocardiograms.

Hanashiro and Weil¹⁴ have reported 2 cases in anaphylactic shock carefully followed with hemodynamic and metabolic studies. The first patient was admitted 4 hours after she had received an aqueous estrogen injection. The electro-

cardiogram revealed S-T depressions suggestive of myocardial ischemia. Similar electrocardiographic changes were noted in the second patient, who was admitted 22 hours after an intramuscular injection of procaine penicillin and dihydrostreptomycin.

CASE REPORTS

Case 1. Patient W. B.

A 59-year-old man was admitted to the hospital because of a constricting pain in his chest radiating into the left arm, accompanied by nausea and profuse perspiration. He also complained of generalized itching over his entire body. About 2 hours prior to admission his family physician had treated him with 600,000 units of procaine penicillin, intramuscularly, for acute bronchitis. The patient denied any previous allergies or history of sensitivity to penicillin or any other drug. Within a minute or 2 after the injection, he became anxious, complained of feeling dizzy, and had some itching of the skin, difficulty in breathing, and an urge to defecate. His physician immediately placed him in a recumbent position, gave him 0.3 c.c. of 1:1,000 epinephrine intramuscularly and followed this with 100 mg. of Benadryl intramuscularly. A few minutes later another 0.3 c.c. of epinephrine was injected because the

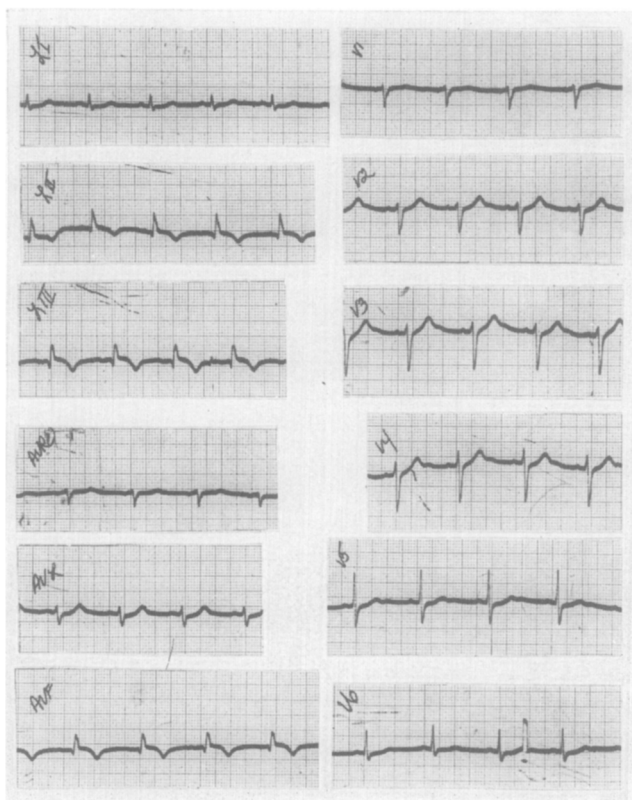


Fig. 1

Patient W. B. (2/14/57). Electrocardiograms indicate a recent inferior wall myocardial infarction.

respiratory distress continued. During the next half hour he felt progressively better and was well enough to return home.

A routine electrocardiogram taken about 7 months previously had been normal. There was no family history of coronary disease, hypertension, or diabetes.

Physical examination showed: blood pressure, 126/60; pulse, 75; respiration, 24; and temperature, 100° F. There was a generalized urticarial rash covering the entire body. The lungs were normal to percussion, but on auscultation there were many rhonchi and prolongation of expiration heard bilaterally. The heart sounds were difficult to evaluate because of wheezing. An infusion of 1,000 c.c. of 5 per cent glucose in distilled water containing 40 mg. of adrenocorticotropic hormone and 1 Gm. of aminophylline was given over an 8 hour period. He was started on heparin parenterally, and, in view of the severe chest pain, 100 mg. of Demerol was given intramuscularly. He was also placed in an oxygen tent. During the next few hours the patient appeared to improve. The rash subsided, his breathing became less labored, and he no longer complained of any chest pain. He remained in the hospital for 3 weeks, and the remainder of his course was uneventful.

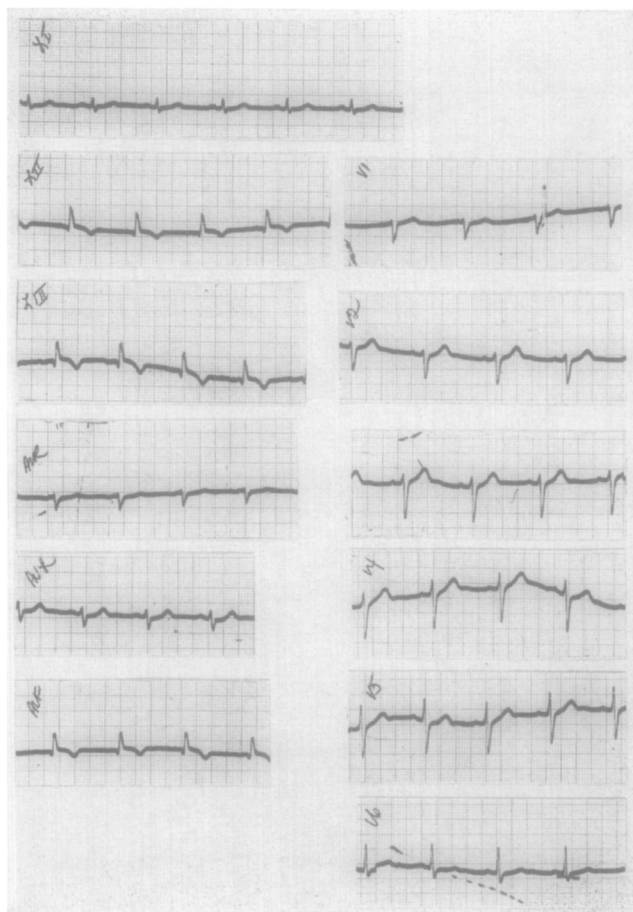


Fig. 2

Patient W. B. (2/26/57). Electrocardiograms still show signs (inversion of the T waves in leads II, III, and AVF) of a recent inferior wall myocardial infarction.

Laboratory findings on admission were: hemoglobin, 15 Gm.; hematocrit, 45 per cent; and leukocyte count, 11,300 with 73 per cent polymorphonuclear leukocytes, 18 per cent lymphocytes, 2 per cent monocytes, and 7 per cent eosinophils. Urinalysis was normal. Sedimentation rate was 33 mm. per hour. (This reaction to penicillin occurred prior to the introduction of serum enzyme determinations for the diagnosis of myocardial infarction.)

After remaining home for about half an hour the itching of the skin returned, spreading almost over the entire body; and at this time he also complained of the severe constricting chest pain. The patient was hospitalized for 3 weeks. In the past he had never complained of any previous angina, although he worked as a salesman carrying brief cases weighing 10 to 15 pounds and often walked up stairs without any distress.

Roentgenogram of the chest prior to discharge from the hospital showed a heart size at the upper limits of normal and accentuation of the linear markings at both bases.

The electrocardiogram (Figs. 1 and 2) was consistent with acute inferior wall myocardial infarction. About 3 months following the admission to the hospital the patient was seen at the office for a routine follow-up examination. During the interval he had no complaints. He was able to walk many blocks without any distress, although he did not return to his occupation as salesman. The electrocardiogram at that time had returned to normal. The

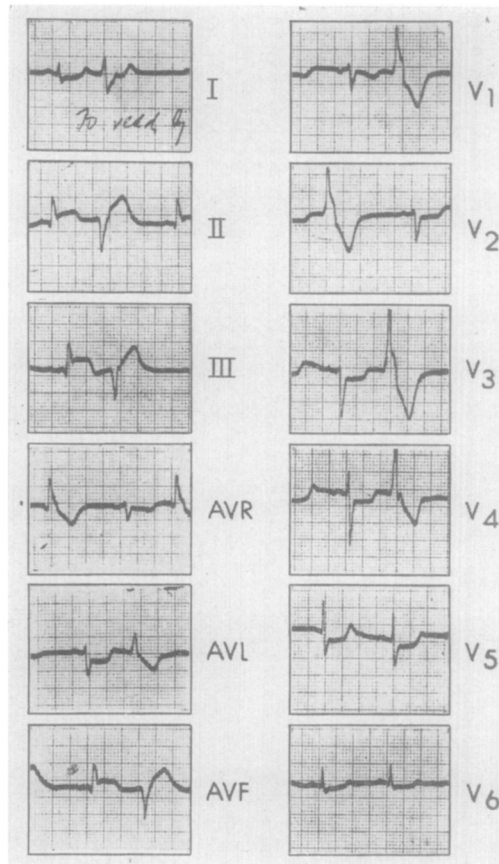


Fig. 3

Patient R. W. (2/13/57). Electrocardiograms show the pattern of a quite recent inferior wall myocardial infarction and frequent unifocal ventricular premature contractions.

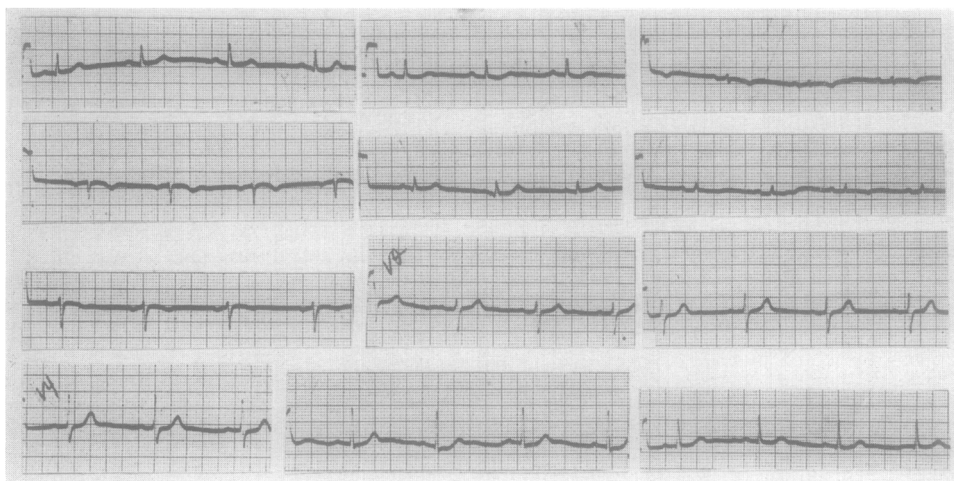


Fig. 4
Patient W. J. (11/21/65). Electrocardiograms are within normal limits.

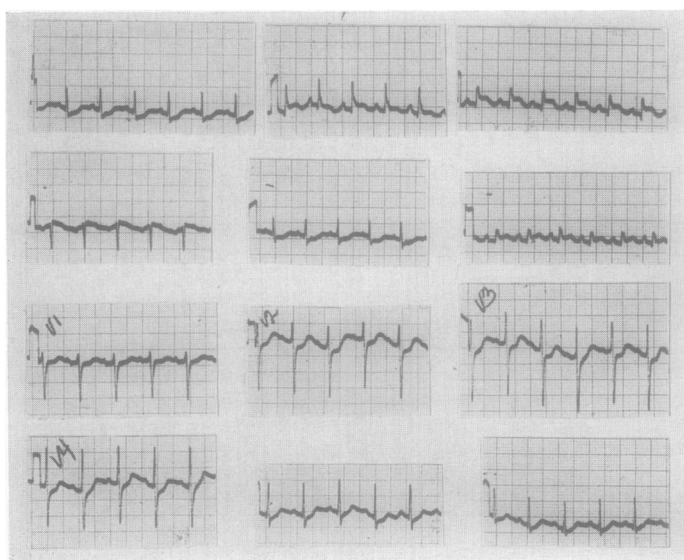


Fig. 5
Patient W. J. (11/28/65). Electrocardiograms show sinus tachycardia and a recent inferior wall myocardial infarction.

patient subsequently had a fatal myocardial infarction that occurred at rest 4 years after his initial episode.

Case 2. Patient R. W.

This 42-year-old woman sustained a dog bite of the hand on Sept. 2, 1960. She was treated at the emergency ward of a local hospital, where she was given tetanus antitoxin and 600,000 units of aqueous penicillin intramuscularly. Five days later she started to complain of itching skin and pain in the wrists, elbows, shoulders, and knees, followed in a few hours by pressing chest pain. She was admitted to the hospital.

Physical examination revealed: blood pressure, 100/64, pulse, regular; and respirations, 26. There was a diffuse red mottling of the skin. Otherwise, she appeared to be in fairly good health. There was no dyspnea or cyanosis at rest. Her heart sounds were normal. There was a regular rhythm, and no murmurs were heard. The lungs were clear to percussion and auscultation. There was no ankle edema. The electrocardiogram (Fig. 3) showed S-T and T wave changes in the limb and left precordial leads, indicating a recent posterior wall myocardial infarction. Roentgenogram of the chest was normal.

Laboratory findings were: hemoglobin, 12.4 Gm.; hematocrit, 38 per cent; and leukocyte count, 11,800, with 68 per cent polymorphonuclear leukocytes, 20 per cent lymphocytes, 2 per cent monocytes, and 8 per cent eosinophils. Urinalysis was normal.

She was given 50 mg. of Demerol on admission for her chest pain and was subsequently sedated with Phenobarbital, 32 mg. 3 times a day. After remaining in the hospital for a week, electrocardiograms returned to normal. She felt well and was discharged. She was subsequently followed for 3 years after the admission and had no cardiac complaints.

Case 3. Patient W. J.

This 61-year-old man entered the hospital because of a carcinoma of rectosigmoid (previous biopsy). He tolerated resection of involved area and a colostomy on Nov. 23, 1965. The patient had been prepared preoperatively in the usual manner with neomycin and magnesium sulfate. Two days after the operation he was started on daily penicillin, 10 million units intravenously. There was no known allergy to drugs. On admission the white blood cell count was 10,200 with a normal differential. On the day after surgery (Nov. 24) it was 15,400. On Nov. 29, the white count had risen to 50,000 with an increase in polymorphonuclear leukocytes. On Dec. 6 it was 16,400, and on Dec. 17 it returned to the preoperative figure of 10,700. On Nov. 27, the patient developed diffuse erythematous urticarial lesions on the face, limbs, and trunk. On the following day, while being taken to the sitz bath, he complained of chest pain and fainted. Blood pressure was 100/70. The electrocardiograms (Figs. 4 and 5) taken on the following day revealed evidence of a recent posterior wall myocardial infarction. On Nov. 29, the eruption covered the entire body and in some areas was desquamating in large sheets. He was immediately placed on prednisone (10 mg. four times daily). This was continued in decreasing doses daily until Dec. 5, when it was stopped. By Dec. 3, the skin showed a fairly normal appearance.

DISCUSSION

Involvement of the heart in acute allergic reactions in experimental animals is well documented by investigators such as those cited previously.^{1-10, 15, 16} The clinical occurrence of cardiac abnormalities in association with allergic reactions to drugs has been reported over a period of many years,^{11-14, 17} but the relatively scant attention paid to this possibility has prompted this report. Unfortunately, in a life-threatening disease such as myocardial infarction, it is not possible to carry out some types of studies which ordinarily might be employed to exclude a chance association between the allergic drug reaction and the cardiac disease. However, the sequence of events in the cases reported is very suggestive, and

Booth and Patterson¹⁷ have recently reported a patient who had electrocardiographic evidence of myocardial ischemia following the administration of penicillin on two occasions. Some of these patients, such as our first case, may well have underlying coronary artery disease, and myocardial infarction in some instances may result from hypotension during acute severe allergic reactions. Sympathomimetic drugs used to treat the allergic reactions may also be of importance in some cases. There appears, however, to be a very real possibility that in some instances the heart itself participates in the allergic reaction to drugs.

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