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Hypertrophic obstructive cardiomyopathy with pseudo-myocardial infarction pattern

A case report

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Summary

A 60-year-old woman with mild hypertension and presumed ischaemic heart disease was followed up over a very long period on account of angina pectoris. Acute myocardial infarction (MI) was suspected on the basis of the history, ECG findings and serum enzyme values, but disproved by radio-isotope investigation. Echocardiography demonstrated features of hypertrophic obstructive cardiomyopathy (HOCM), a diagnosis supported by cardiac catheterization and endomyocardial biopsy (EMB). Histological features of HOCM were absent from left ventricular EMB specimens despite a significant intraventricular gradient, but the right ventricular EMB demonstrated extensive changes of HOCM despite a small intraventricular gradient. Cardiac catheterization excluded previous MI and coronary artery disease. A further interesting feature was the development of congestive cardiac failure, which necessitated modification of her drug therapy.)

S Afr Med J 1968; **69:** 828-832.

Case report

This 60-year-old, obese, white woman had been treated for hypertension and angina pectoris for some 20 years. There was also a history of hypercholesterolaemia and thyrotoxicosis necessitating a subtotal thyroidectomy in 1965. Her father had died from diabetes mellitus. The patient was taking a great number of drugs which included atenolol, isosorbide dinitrate orally and sublingually, dipyridamole, clofibrate, aspirin, a diuretic and a sedative. Approximately 1 week before admission to the Intensive Coronary Care Unit (ICCU) at Tygerberg Hospital she was admitted to a private hospital for 'sciatica', and there experienced severe chest pain followed by syncope. The ECG taken at that time was reported as showing 'nonspecific T-wave changes' and the serum lactate dehydrogenase level was reputedly slightly raised. She was discharged from the private hospital after 2 days but a few days later was awoken suddenly with a severe crushing precordial pain slightly relieved by sublingual nitrates.

She was admitted to Tygerberg Hospital ICCU on 29 November 1984. On interrogation her only other significant symptoms were grade II dyspnoea, lethargy and palpitations not related to effort. Assessment of the cardiovascular system elicited a regular right radial pulse with no abnormality. The remaining peripheral pulses were fairly weak and the jugular venous pressure was not elevated. The blood pressure was 120/80 mmHg with significant postural decrease. There was evidence of left ventricular (LV) cardiomegaly; the apex beat was forceful and in the 6th intercostal space in the anterior axillary line. The 1st and 2nd heart sounds were normal but there was a prominent LV 4th heart sound. A grade 3/6 midsystolic murmur was clearly audible at the mitral area with some radiation up the left parasternal region and axilla. She had grade I hypertensive retinopathy. Side-room investigations were all negative. A chest radiograph delineated slight LV cardiomegaly. A resting ECG recorded while the patient was experiencing chest pain revealed sinus rhythm of 100/min, a P-R interval of 0,12 second, mean QRS axis of +10°, and LV hypertrophy by voltage criteria with anterolateral 2-3 mm horizontal ST-segment depression due to either a 'strain pattern' or possible acute nontransmural myocardial infarction (MI). Furthermore, there was very poor R-wave progression in the anteroseptal leads indicative of a pseudo-infarction pattern of LV hypertrophy or myocardial ischaemia. No atrial enlargement could be seen. A resting ECG, done after relief of chest pain by sublingual isosorbide dinitrate, indicated far less ST-segment depression anterolaterally.

The clinical diagnosis was of a possible acute nontransmural anterolateral MI with mitral incompetence secondary to papillary muscle dysfunction. Heparinization was instituted, as were maintenance nitrates, nifedipine 10 mg 3 times daily, and atenolol 50 mg/d. Later during the day the patient suddenly

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developed atrial fibrillation with a rapid ventricular response associated with some further chest pain and dyspnoea. After digitalization the rhythm reverted to normal with symptom relief. Two days later she had a further episode. A resting ECG during this episode showed QS waves accompanied by 1,5 mm ST-segment elevation in leads V1 - V3 with deeply inverted P waves in these leads. Some 2 mm ST-segment depression was seen in leads I, II, aVL, V5 and V6. Another remarkable feature was bi-atrial enlargement. At this stage a nitroglycerin infusion gave rapid relief of her chest pain, and an ECG now showed the reappearance of R waves anteroseptally, almost normal P waves, and persistent ST-segment depression. Daily serial ECGs demonstrated no real further change but serial cardiac enzyme determinations depicted the pattern of a classic acute MI. Since the clinical diagnosis was uncertain, a technetium-99m pyrophosphate scintiscan ('hot-spot scan') was carried out on 6 December 1984 but proved negative, and thus left the diagnosis of an acute MI in doubt. The further hospital course was uneventful and the patient was discharged on 10 December on the following medication: nifedipine 10 mg 3 times daily, digoxin 0,25 mg/d, isosorbide dinitrate 40 mg 3 times daily, atenolol 50 mg/d and sublingual nitrates when necessary.

On 22 December she was readmitted with a 3-day history of grade III dyspnoea, orthopnoea and ankle swelling but no chest pain. Clinical examination indicated biventricular cardiac failure in addition to mitral insufficiency. A chest radiograph confirmed moderate pulmonary oedema but there was now most significant LV cardiomegaly. A resting ECG showed bi-atrial enlargement, poor R-wave progression anteroseptally, and anterolateral ST-segment depression with digitalis effect. The cardiac failure was managed and a second acute MI was excluded by serial serum enzyme determination and ECG. The likelihood of hypertrophic obstructive cardiomyopathy (HOCM) was considered, and M-mode and two-dimensional echocardiography was performed; this confirmed the diagnosis of HOCM in that there was gross systolic anterior motion of the anterior mitral leaflet, asymmetrical septal hypertrophy with an interventricular septum: LV posterior wall thickness ratio of 2,2, systolic fluttering and midsystolic closure of the aortic valve. The left atrium was also moderately dilated and the ejection fraction was 54%. Two-dimensional echocardiography showed no areas of previous MI. A 24-hour Holter recording only demonstrated infrequent atrial ectopic activity.

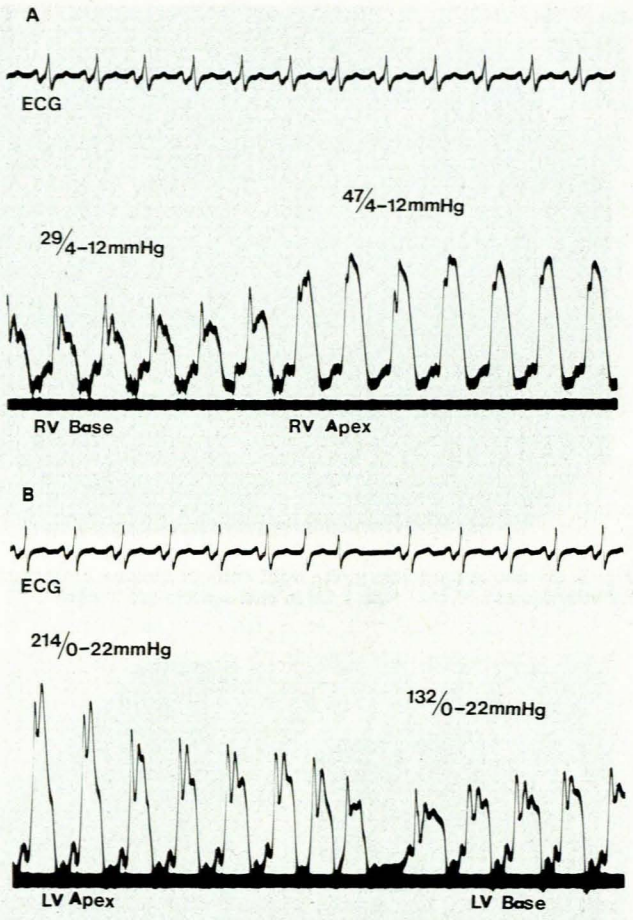

Fig. 1. Pressure tracings in mmHg recorded at rest within the RV and LV. A — intraventricular gradient of 18 mmHg in the RV on withdrawal of catheter from the base to the apex; B — intraventricular gradient of 82 mmHg in the LV on advancing the catheter from the apex to the base. Note the single ectopic beat.

Cardiac catheterization

Cardiac catheterization was undertaken on 3 January 1985. The intracardiac pressures recorded (all in mmHg) were as follows: right atrium — mean 11; right ventricle (RV) — low 47/4-12, high 29/4-12; main pulmonary artery — 29/18 (mean 25); pulmonary capillary wedge — mean 22; LV — low 214/0-22, high 132/0-22; and central aorta — 132/72 (mean 112). Further haemodynamic data were as follows: LV dp/dt 2 627 mm/s; cardiac output 5,7 l/min; cardiac index 2,7 l/min; systemic vascular resistance 17,7 U; pulmonary vascular resistance 2,3 U. These results were thus in keeping with HOCM with a resting RV gradient of 18 mmHg (Fig. 1, A) and a resting LV gradient of 82 mmHg (Fig. 1, B). LV cine angiography in the right anterior oblique (Fig. 2) and left anterior oblique projections delineated classic features of HOCM with additional non-calcific and mild mitral insufficiency. There was no evidence of previous MI. RV cine angiography in the right anterior oblique view demonstrated a markedly hypertrophied chamber which was hypercontractile and in keeping with HOCM involving the right side of the heart (Fig. 3). Aortic cine angiography in the left anterior oblique projection showed a moderately calcified ascending aorta with a non-calcified aortic valve (three cusps) and mild aortic insufficiency. Injection of dye into the right coronary artery (RCA) showed this to be a large and dominant vessel free of atherosclerotic lesions, with markedly tortuous branches and an increased flow. The left coronary artery (LCA) had a high blood flow with no obstructions, but marked systolic compression of the septal perforators. Multiple RV and LV endomyocardial biopsy (EMB) specimens were obtained.

Histological features of EMB specimens

LV biopsy. On light microscopy the myocardium appeared definitely hypertrophied with enlargement of the nuclei of the mycocytes. Electron microscopy confirmed the presence of hypertrophy with enlarged and at times crenated cardiac nuclei. Despite extensive sampling, myofibrils were normally aligned and no evidence of myofibrillar disarray could be found. Other features included lipofuscinosis and mitochondriosis (Figs 4 and 5).

RV biopsy. Hypertrophy of the myocardial cells was obvious on light microscopy. Electron microscopy showed obvious myofibrillar disarray in many of the blocks examined (Figs 6 and 7). Myofibrils ran at angles to one another in varied directions. Myofilaments of one myofibril could be seen to diverge from the parent myofibril and be inserted at an angle into the Z band of an adjacent myofibril.

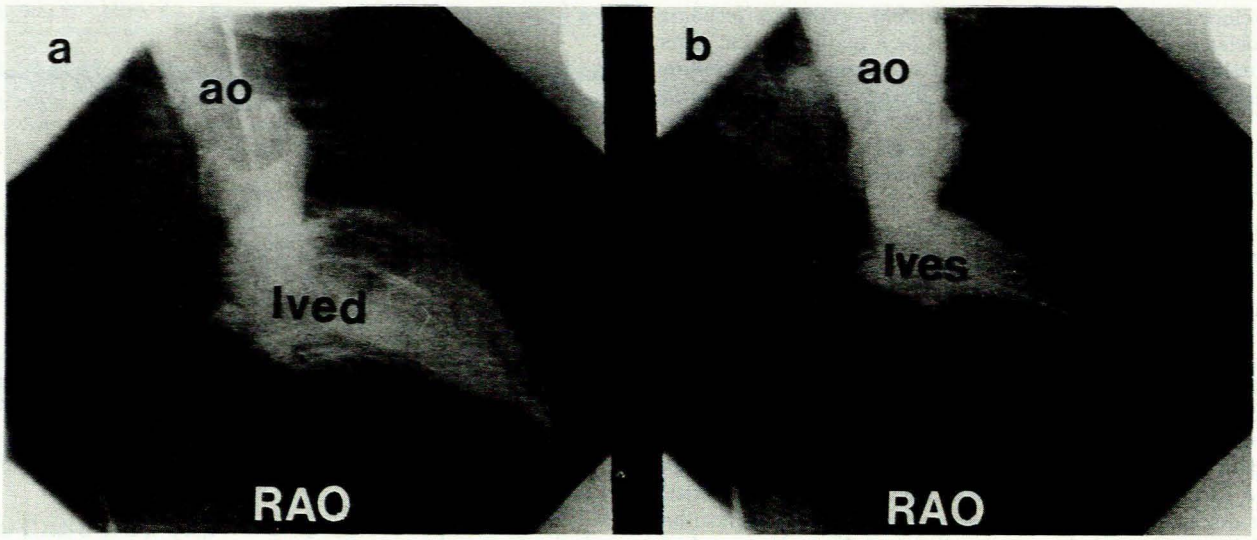

Fig. 2. LV cine angiograms in the right anterior oblique projection. Typical features of HOCM with mild mitral insufficiency. a — lved = LV in end-diastole; b — lves = LV in end-systole (ao = aorta).

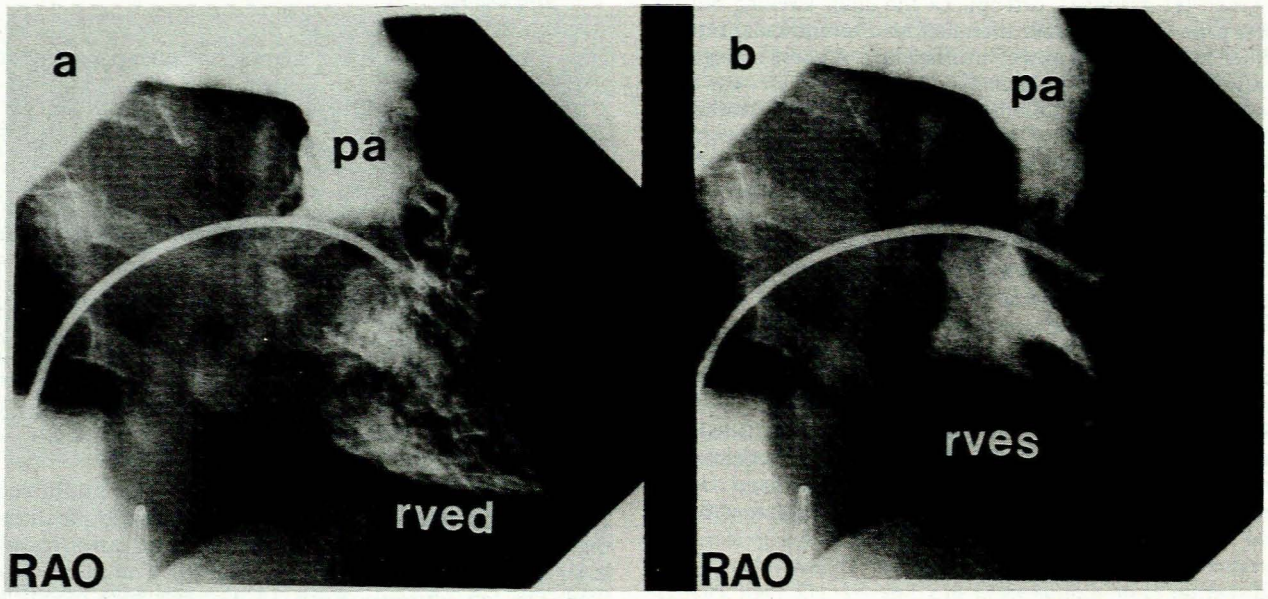

Fig. 3. RV cine angiograms in the right anterior oblique projection. A markedly hypertrophied ventricle which is hypercontractile is visualized. a — rved = RV in end-diastole; b — rves = RV in end-systole (pa = pulmonary artery).

Follow-up

A definitive diagnosis of HOCM involving both ventricles was established, with no coronary arterial obstruction and no evidence of previous MI, but with the complication of cardiac decompensation as evidenced by significant cardiac dilation. The patient was discharged on 11 January 1985 and maintained on digoxin, diuretics, aldosterone antagonists and a small dose of a β-blocker. She was last seen on 13 February 1985 and has continued to feel very well apart from some tiredness and grade I dyspnoea. She has not experienced any further syncopal episodes or angina pectoris. Repeated 24-hour Holter monitoring failed to detect any significant arrhythmia.

Discussion

This case brings into focus several controversial aspects. Angina pectoris is a common symptom of patients with HOCM, and the usual explanation is that there is such extensive myocardial hypertrophy that the coronary circulation cannot keep pace with metabolic demands of the myocardium. Several such patients were young and without obstructive atherosclerotic coronary artery disease. In fact, very large patent coronary arteries with markedly increased flow rate are classic signs of HOCM.[1] Some researchers[2] believe that an abnormality of ventricular wall dynamics is responsible for the angina. A most interesting coronary angiographic observation in HOCM has been that of systolic compression or 'milking' of the septal perforator vessels coursing in the hypertrophied interventricular septum,[3,4] a phenomenon clearly demonstrated in our patient. The exact role of this compression in the pathogenesis of myocardial ischaemia is not clear, especially since coronary blood flow is greatest in diastole. A few years ago, a further possible mechanism for angina was revealed by the demonstra-

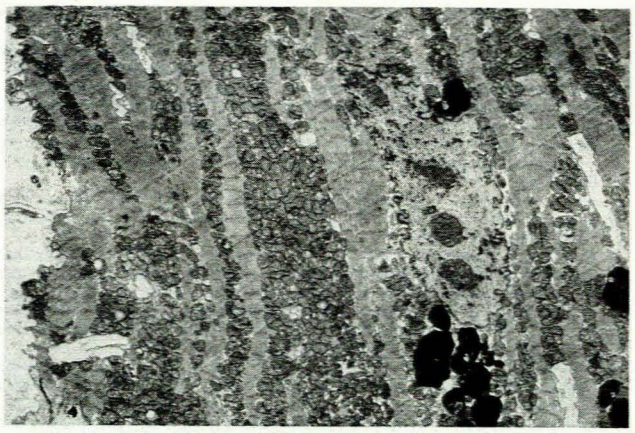

Fig. 4. Electron photomicrograph (EM) of LV EMB specimen showing hypertrophy with crenated nucleus, obvious mitochondriosis, and electron-dense perinuclear lipofuscin. There is no myofibrillar disarray (uranyl nitrate and lead citrate stain x 5 000).

Fig. 6. EM of RV EMB specimen. In this myocyte there is complete myofibrillar disarray with myofibrils running in all directions instead of their normal parallel orientation (uranyl nitrate and lead citrate stain x 5 000).

Fig. 5. EM of LV EMB specimen showing hypertrophied myocyte with enlarged nucleus and some degree of mitochondriosis but no significant myofibrillar disarray (uranyl nitrate and lead citrate stain x 7 000).

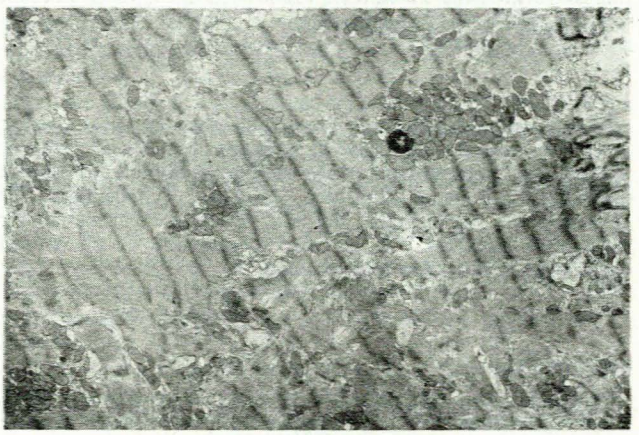

Fig. 7. EM of RV EMB specimen. Less marked myofibrillar disarray seen in another block (uranyl nitrate and lead citrate stain x 8 000).

tion of symptomatic coronary artery spasm in this disease,[5] perhaps due to abnormal responsiveness to catecholamines, believed by some to be the cause of HOCM. The presence of 'muscle bridges', especially those coursing over the left anterior descending coronary artery, may be a factor in myocardial ischaemia and angina pectoris, as well as acute MI.[6] Both Newman[7] and Maron *et al.*[8] have documented the complication of acute MI in HOCM with angiographically normal coronary arteries. Przybojewski *et al.*[9] reported recurrent acute MI in a patient with HOCM and associated syphilitic coronary arteritis in whom coronary vasospasm may well have played a role. Interpretation is complicated by the fact that atherosclerotic coronary artery disease may coexist with HOCM.[10,11]

Our case also illustrates the difficulty in excluding previous MI (and even acute MI) in patients with HOCM, often due to the occurrence of 'pseudo-myocardial infarction patterns' on ECG.[12] Poor R-wave progression or the presence of Q waves in the anteroseptal leads, secondary to LV hypertrophy, can mimic acute anteroseptal MI in 20% of patients with HOCM. Intermittent left atrial enlargement was well documented in the present case and is probably an indication of dynamic changes in LV compliance characteristics.[13] Acute atrial fibrillation, a common arrhythmia in HOCM which invariably results in profound haemodynamic deterioration, was also encountered but fortunately was short-lived.

The use of percutaneous EMB in the diagnosis of HOCM is somewhat controversial. In the early stages LV EMB could be more reliable than RV sampling.[14,15] This generally accepted belief did not hold true in our patient since histological features of HOCM were documented on RV EMB but not in LV specimens ('sampling error'). It is generally conceded that there is no 'pathognomonic' histological picture in HOCM and that the diagnosis must be established in conjunction with other criteria — clinical, echocardiographic and haemodynamic. Myofibrillar and myofibre disarray was striking in the RV biopsy samples and this finding is thought by Alexander and Gobel[16] to be highly specific for HOCM, although others[17–19] are unimpressed with this specificity.

Intraventricular pressure gradients at rest were far more impressive in the LV than in the RV (Fig. 1). A diagnosis of HOCM, based solely on the demonstration of such a gradient, is unwise since non-obstructive mechanisms can cause such gradients and their exact pathophysiology is uncertain. Nevertheless, this haemodynamic finding is useful in establishing a diagnosis of HOCM with the additional clinical, echocardiographic and EMB features. Gradients within the LV are far more common than in the RV, in which this is documented in approximately 15% of cases.[1] The haemodynamic and prognostic significance of such gradients is doubtful.

Congestive cardiac failure (CCF), usually also associated with supraventricular arrhythmias, as in our patient, is usually considered an ominous occurrence in the natural history of HOCM. The development of CCF is relatively unusual and usually signifies the 'end-stage' of the disease. Progression to LV dilatation with ensuing CCF was first reported by ten Cate and Roelandt,[20] and this complication was also alluded to by Shah *et al.*[21] However, Oakley,[22] Goodwin[23–25] and Maron *et al.*[8] have not been able to verify the pathological features of dilated (congestive) cardiomyopathy (COCM) in patients with HOCM who died of CCF, and doubt strongly the possibility of HOCM deteriorating into COCM. The EMB specimens in our patient certainly did not demonstrate findings usually described in COCM, although these are not pathognomonic of the disease.

In conclusion, it was of great importance to exclude obstructive coronary artery disease as well as acute MI in this patient. This misdiagnosis, together with CCF, would have led to the institution of medical therapy which could have aggravated the underlying HOCM; it was also important to appreciate the development of CCF because medication must be modified to improve symptoms. However, prognosis in this clinical situation would appear to be unfavourable.

We sincerely wish to thank Miss H. W. Weymar of the Cardiac Unit for preparing the ECG illustrations, and Mr Christopher Wilberforce, formerly head of the the Photographic Unit, Bureau for Medical and Dental Education, University of Stellenbosch, for preparing the photographs. We also appreciate permission for publication from Dr J. P. van der Westhuyzen, Chief Medical Superintendent of Tygerberg Hospital.

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News and Comment/Nuus en Kommentaar

Handel, Bach and eye surgery

The two celebrated composers, Handel and Bach, both went blind in their later years. Bach had been myopic all his life and presumably later developed a cataract. Whether Handel suffered from cataract or glaucoma is an open question. However, both were victims of the celebrated charlatan, Chevalier John Taylor (1703-1773), who travelled the Continent professing to have an unparalleled knowledge of ophthalmology, which he certainly did not possess. It is highly probable that he destroyed the sight of many unfortunate victims, but since he moved around fairly fast the discovery that an operation on the eye had been totally unsuccessful tended to occur after his departure.

Lindeboom (*Ned Tijdschr Geneeskd* 1985; **129:** 2458) has recently recounted the misadventures of Bach and Handel at the hands of this charlatan who had served as an apprentice to an apothecary in London and then studied medicine at St Thomas's Hospital. His life is a proof of the power of advertising. His arrival in any city was heralded by announcements in the newspapers, distribution of pamphlets and so on, while his entry into the city was usually in a beautiful coach with outriders and trumpeters. Many members of the aristocracy were taken in by his charming manners, but Frederick the Great was not deceived and threatened to hang Taylor if he touched any of his subjects.

Handel had already been operated upon in 1752 by William Bromfield of St George's Hospital, presumably for cataract, without success and he was later treated by Taylor who quickly declared the situation hopeless. Although Taylor claimed success for his operation on Bach, the facts are otherwise. Bach was persuaded against his will to have his eye operated upon at home, but when the bandage was removed 5 days later his sight was worse and he was having a great deal of pain, probably due to an infection. A second operation was equally unsuccessful, and merely added to Bach's misery. A few months later a stroke carried him off.