Cardiac Manifestations of Malignant Hyperthermia Susceptibility

VICTOR F. HUCKELL, M.D., F.R.C.P. (C), HOWARD M. STANILOFF, M.D., F.R.C.P. (C), BEVERLEY A. BRITT, M.D., F.R.C.P. (C), MENASHE B. WAXMAN, M.D., F.R.C.P. (C) AND JOHN E. MORCH, M.D., F.R.C.P. (C)

SUMMARY Malignant hyperthermia is a disease resulting from defective cellular membranes, usually presenting as drug-induced pyrexic crises. We describe four patients with life threatening ventricular arrhythmias or chest pain in the absence of pyrexic crises. Three presented with life threatening arrhythmias and the fourth with severe atypical chest pain. Two patients had a family history of multiple sudden deaths. Resting CKs were elevated in three patients while CK-MB was elevated in one. Resting ECGs were abnormal in three. Three patients had recurrent ventricular tachycardia, two had recurrent ventricular fibrillation and multiple cardiac arrests. Cardiac catheterization showed abnormal left ventricular wall motion in two and minimal mitral valve prolapse in one while all had normal coronary arteries. Thallium-201 myocardial imaging demonstrated large perfusion defects in the patient with electrocardiographic Q waves and normal coronary arteries.

Myocardial involvement has been demonstrated by clinical, electrocardiographic, hemodynamic, angiographic and myocardial imaging abnormalities. Malignant arrhythmias occurred in these patients in the absence of pyrexic crises or drug administration. Abnormal calcium release in the myocardium, as documented in skeletal muscle membranes, may be a unifying concept for the various manifestations described.

MALIGNANT HYPERTERHANIA (MH), regarded as a rare disease most often encountered by anesthetists, is an inherited disease of skeletal muscle1-4 in which hyperthermic crises may be produced by potent inhalational anesthetics, skeletal muscle relaxants or certain local anesthetics.4 5 Some reports suggest that crises may also be precipitated by nonpharmacologic events such as severe emotional or physical stress or high environmental temperature.1-4 During crises, patients may show high fever, muscle rigidity, tachycardia and/or ventricular arrhythmias, hyperventilation, hypotension, mottled cyanosis and sudden death.1-4 Ventricular arrhythmias are frequently the terminal event in an anesthetic-induced malignant hyperthermic reaction, and postmortem studies show myocardial necrosis in these patients. Susceptibility to these crises is diagnosed by skeletal muscle biopsies in which the skeletal muscle is exposed to caffeine and caffeine plus halothane with measurements of isometric or resting tension.4, 5 Muscles from patients susceptible to malignant hyperthermia exhibit marked increases in contracture after exposure to these agents. In addition, there are light and electron microscopic changes highly suggestive but not diagnostic of the disease.8-12 These patients are considered to have malignant hyperthermia susceptibility (MHS) even if they have never had elevated temperatures or pyrexic crises. Our purpose is to describe the presenting cardiac manifestations of four patients never having had elevated temperatures. Three of these patients were studied because of a suspicion that ventricular arrhythmias may be related to MHS in selected patients in the absence of hyperthermic crises. The fourth was studied because of cardiac symptoms in association with a strong family history of anesthetic associated deaths.

Methods

Examination of skeletal muscle biopsies was carried out according to techniques described in previous publications.6, 7 In brief, muscle fascicles were secured at each end with black silk sutures and then meticulously dissected free from the surrounding muscle while maintaining constant tension on the sutures in such a manner as to preserve the whole cells free from contractures or excessive stretching. The fascicles were then immediately transported to the laboratory in ice-cold Ringer’s solution. The time elapsed between excision and further processing in the laboratory was about 10 minutes. The specimens were trimmed free of any irregularities or remaining fat and each was divided into two pieces to permit measurements in duplicate. The size of each muscle strip was approximately 3 x 5 x 20 mm, each weighing roughly 0.3 g with a range from 0.2-0.4 g. In trimming the muscle, care was taken to ensure that the direction of the long cut ran parallel to the fibers. Each muscle strip, secured by a silk suture to an electrode housing, was immersed in 30 ml of a Krebs Ringers solution at pH 7.4 adapted for human tissues. The upper end of the muscle was connected via a second silk suture to a Grass force displacement transducer (ST-10-DC). Isometric tension was recorded with a Grass polygraph. The initial tension was set at 0.5 or 1 g (the magnitude of the contracture was not altered by changing the baseline tension from 916
0.5 to 1 g). In order to assess viability, the muscle was stimulated every 5 seconds via platinum electrodes connected to a square wave Grass stimulator which was set to deliver 8-V impulses of 20 msec duration. Oxygen containing 5% carbon dioxide (carbogen) was bubbled through the bath at 1 l/min. The temperature was maintained at 37°C through all studies. Caffeine, known to increase release of calcium from the sarcoplasmic reticulum, was added directly to the bath in increments from 2–32 mM. Each caffeine dose was left in the bath for 5 minutes and then removed and replaced by a dose double that of the previous dose. The parameter measured was the contracture expressed as grams of tension increase produced 4 minutes after the addition of each dose of caffeine. Once the maximum contracture of which the muscle was capable was reached, the caffeine was removed by repeated washing. The muscle was then equilibrated for 30 minutes with 1 vol% halothane added via the carbogen line. Caffeine was then again added, this time in increments ascending from 0.25–8 mM. The gram tension increase for each dose was then measured as before.

From the concentration response curves, it is possible to calculate the concentration of caffeine in mM required to raise the resting tension of the isometric skeletal muscle preparation by 1 gm. Figures 1 and 2 demonstrate the clear separation of responses characteristically seen between normals and patients susceptible to MH. This test was used on the four patients described below.

**Results**

Four patients (table 1) presented to cardiologists because of cardiovascular manifestations rather than anesthetic catastrophes. Three patients underwent skeletal muscle biopsy as part of a ventricular arrhythmia investigation protocol while the fourth patient was biopsied because of a family history of sudden death. None of the four patients had had a hyperthermic reaction. All were proven to have MHS by caffeine and caffeine plus halothane contracture tests performed on skeletal muscle biopsies (table 2). Characteristic light and electron microscopic changes were seen in all four patients. All had an increase in small angular fibers with significant variation in fiber diameters. All had variable atrophy of Type I fibers with an increased Type I/II fiber ratio. In addition, all had internal nuclei in many of the hypertrophied fibers. All except patient number four had mild fibrillar degeneration. On electron microscopy, patient number one had dilatation of the sarcoplasmic reticulum with excessive lipid droplets between the myofibrils. Patient number two exhibited variation in the width of the transverse reticulum of the sarcoplasmic reticulum triads. The

![Caffeine](image)

**Figure 1.** A comparison of resting tensions (in grams) of skeletal muscle biopsies characteristic of normal and malignant hyperthermia-susceptible (MHS) patients in response to increasing doses of caffeine. Numbers represent caffeine concentration in mM. Time scale represents duration of exposure to the indicated agents.
Normal

MHS

Figure 2. Resting tension response curves (in grams) characteristic of normal and MHS patients in response to increasing doses of caffeine in the presence of 1 vol% halothane. Numbers represent caffeine concentration in millimoles. Time scale represents duration of exposure to the indicated agents.

Table 1. Clinical Data on Patients with Malignant Hyperthermia Susceptibility

<table>
<thead>
<tr>
<th></th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>37</td>
<td>19</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Sex</td>
<td>male</td>
<td>female</td>
<td>female</td>
<td>female</td>
</tr>
<tr>
<td>Presenting feature</td>
<td>atypical chest pain, fatigue on exertion</td>
<td>multiple episodes of VT and VF</td>
<td>multiple episodes of VT and VF, diplopia</td>
<td>atypical chest pain, diplopia</td>
</tr>
<tr>
<td>History</td>
<td>S4, systolic ejection murmur II/VI at LSB</td>
<td>midsystolic click late systolic murmur</td>
<td>strabismus</td>
<td>S3, S4, I/VI midsystolic murmur at apex, proximal myopathy, strabismus</td>
</tr>
<tr>
<td>Physical</td>
<td>quinidine fever and thrombocytopenia</td>
<td>normal</td>
<td>long QT</td>
<td>inferior and anterior ischemia, multifocal VPBs</td>
</tr>
<tr>
<td>Drug reactions</td>
<td>none</td>
<td>quinidine fever</td>
<td>none</td>
<td>quinidine fever</td>
</tr>
<tr>
<td>Resting ECG</td>
<td>RBBB and LAHB</td>
<td>normal</td>
<td>long QT</td>
<td>inferior and anterior ischemia, multifocal VPBs</td>
</tr>
<tr>
<td>CK (IU)</td>
<td>75</td>
<td>57</td>
<td>38</td>
<td>267</td>
</tr>
</tbody>
</table>

Upper limits of normal for CK values in our laboratory are 60 IU for males and 50 for females.
Abbreviations: CK = creatine phosphokinase; IU = international units; LAHB = left anterior hemiblock; LSB = left sternal border; RBBB = right bundle branch block; VF = ventricular fibrillation; VPB = ventricular premature beat; VT = ventricular tachycardia.
TABLE 2. Muscle Caffeine-Contracture Studies in Patients with Malignant Hyperthermia Susceptibility

<table>
<thead>
<tr>
<th></th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>Normal†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine*</td>
<td>7.9</td>
<td>7.6</td>
<td>7.4</td>
<td>5.9</td>
<td>&gt;9</td>
</tr>
<tr>
<td>Caffeine and Halothane‡</td>
<td>1.1</td>
<td>1.1</td>
<td>1.03</td>
<td>1.0</td>
<td>&gt;1.4</td>
</tr>
</tbody>
</table>

*μM caffeine required to increase resting tension of skeletal muscle by one gram.
†Normals are for our laboratory (20).
‡μM caffeine required to increase resting tension of skeletal muscle by 1 g in presence of 1 vol % halothane.

electron microscopic findings in patients number three and four were also nonspecific. Figure 3 is a representative example of light microscopic findings on skeletal muscle biopsy.

Case 1

A 37-year-old male (table 1) complained of marked fatigue and episodes of resting chest pain, atypical for ischemia, for two years. The pain was sharp and retrosternal in location and radiated to the back but not the arms. The pain was not related to exertion, rest, position or emotional stress. There were no known relieving factors for the pain. At least five first cousins (under 30 years of age) had died suddenly when exposed to general anesthetics. On examination he had a left ventricular S4 and a Grade II/VI systolic ejection murmur at the left sternal border. He had had no known drug reactions. The resting ECG showed a right bundle branch and left anterior fascicular block pattern. CKs at rest were mildly elevated at 75 IU.

Cardiac catheterization (table 3) was normal other than minimal elevation of the right ventricular end-diastolic pressure.

Case 2

A 19-year-old female (table 1) with a two-year history of intractable life threatening ventricular arrhythmias, clinically first evident two weeks after a general anesthetic for an appendectomy, had over 40 cardiac arrests requiring defibrillation. As she was adopted, her family history is unknown. On examination, she had a midsystolic click and late systolic murmur. She developed a fever and significant thrombocytopenia after the use of quinidine sulphate. The resting ECG was normal and CKs were minimally elevated at 57 IU. At present, her arrhythmias are controlled by disopyramide (Rhythmodan).

Cardiac catheterization showed a minimal elevation of right and left ventricular end-diastolic pres-

![Figure 3. Light microscopy (×280) of skeletal muscle biopsy. There is a greater than normal variation of fiber diameters with an excessive number of nuclei and internal nuclei (middle left of picture). The larger fibers show apparent splitting (middle right of picture) into fragments, some of which could persist as angulated fibers. All of these findings are nonspecific.](http://circ.ahajournals.org/)

sures and minimal prolapse of the posteromedial scallop of the posterior mitral leaflet without mitral regurgitation (table 3).

Case 3

A 28-year-old female (table 1) with a one-month history of syncope had recurrent ventricular arrhythmias and a cardiac arrest after a flu-like illness. Although her paternal grandmother died suddenly, there was no other family history of sudden death. Her physical examination was normal except for strabismus. The ECG showed a long QT interval. While in the hospital, she had episodes of spontaneous ventricular tachycardia. Cardiac catheterization (table 3) revealed generalized hypokinesis and apical akinesis without mitral regurgitation. Her arrhythmias have been controlled for five years by propranolol. Her CKs were normal on multiple occasions. No significant perfusion defects were seen on thallium-201 myocardial imaging.

Case 4

A 22-year-old female (table 1) had a four-month history of spontaneous ventricular arrhythmias and transient sharp left chest pains. The pains were localized and not related to exertion or rest, position or emotional stress. She had episodic diplopia for several years. There were multiple nonanesthetic-related sudden deaths in the family (vide infra). Biventricular S3 and S4 gallops and a grade II/VI mid-systolic murmur at the apex were heard. She also had a mild proximal skeletal myopathy and latent strabismus. Fever developed on the use of quinidine sulphate. The resting ECG (fig. 4) demonstrated significant Q waves in leads III, aVf, V4 and V5 with left axis deviation. Rhythm monitoring showed frequent multifocal ventricular premature beats which were ultimately controlled by oral procaainamide. The resting serum CK was significantly elevated at 267 IU with an increase in the CK-MB band (table 1).

Cardiac catheterization (table 3) showed minimal elevation of right and left ventricular end-diastolic pressures. A left ventricular angiogram (fig. 5) demonstrated an increased end-diastolic volume (EDV) of 180 ml, with an end-diastolic volume index of 118 ml/m2 (normal < 98 ml/m2). The end-systolic volume (ESV) was increased at 84 ml with an end-systolic volume index of 55 ml/m2 (normal < 27 ml/m2). The ejection fraction was decreased at 53% (normal 60–75%). Apical akinesis was seen.

Thallium-201 myocardial imaging was performed in three views (anterior, left anterior oblique and left lateral) at rest and exercise after injection of 2 mCi of thallium-201. Figure 6 shows anterior and left anterior oblique views with a large apical perfusion defect ex-

| Table 3. Cardiac Catheterization Data on Patients with Malignant Hyperthermia Susceptibility |
|---------------------------------|--------|--------|--------|--------|
|                                | #1     | #2     | #3     | #4     |
| Right atrial mean              |        |        |        |        |
| (< 8 mm Hg)                    | 8      | 7      | 2      | 6      |
| RV end-diastolic pressure      |        |        |        |        |
| (< 5)                          | 6-8    | 7-9    | 2-4    | 6-7    |
| Wedge mean (<12)              |        |        |        |        |
| LV end-diastolic pressure      |        |        |        |        |
| (<12)                          | 10     | 14-16  | 4-7    | 11-14  |
| Cardiac index                  |        |        |        |        |
| (2.5–3.5 l/min/m²)             | 4.2    | 3.5    |        | 3.6    |
| LV angiogram                   | normal | minimal prolapse | generalized hypokinesis, apical akinesis | normal |
| Ejection fraction              |        |        | 73%    |        |
| Coronary arteriograms          | normal | normal | normal | normal |

Abbreviations: LV = left ventricle; RV = right ventricle.
Numbers in parentheses are normals for our laboratory.

Figure 4. Twelve-lead electrocardiogram showing significant Q waves in leads III, aVf, V4 and V5 with left axis deviation. Standardization is normal.
tending up the anterior wall corresponding to the apical akinesis seen on left ventricular angiography (fig. 5) and the Q waves seen on the ECG (fig. 4).

This patient’s family history (fig. 7) was investigated retrospectively. Two brothers and the mother died suddenly. The first brother died at age 16 while walking. His postmortem grossly showed thickening of the anterior and posterior walls of the left ventricle. Microscopically, there was “cellular hypertrophy” with diffuse “chronic scarring and fibrosis” suggestive of “chronic myocarditis.”

The second brother died suddenly at age 18 while skating. The postmortem showed mild ventricular dilatation with “ventricular hypertrophy” and “multi-

Figure 5. Left ventricular angiogram showing apical akinesis with increased end-diastolic (EDV) and end-systolic (ESV) volumes of 180 ml and 84 ml and a decreased ejection fraction (EF) of 53%.

Figure 6. Thallium-201 myocardial images in anterior and left anterior oblique views showing large apical and posterolateral defects.
ple focal areas of muscular degeneration and interstitial fibrosis.”

The patient’s mother died at age 25, ostensibly due to a “postpartum cardiomyopathy.” It is unknown if she had been exposed to anesthetics during her delivery. She was described in a 1963 case report as having “moderate left ventricular hypertrophy” and “generalized foci of inflammation and myocardial degeneration” microscopically. The microscopic changes in these three relatives were similar to those described recently in three patients who had hyperthermic reactions. The living members of this patient’s family had serum CK levels performed. The surviving father, maternal aunt and paternal cousins all have significantly elevated CKs and are currently being evaluated for malignant hyperthermia. The sister has elevated CKs and is MHS on skeletal muscle biopsy.

Discussion

MH is believed to result from defective cellular membrane function. Patients who develop elevated temperatures following exposure to pharmacologic agents are designated as having had malignant hyperthermic crises. However, susceptibility to these crises can be established by skeletal muscle biopsies. These biopsies exhibit characteristic light and electron microscopic changes and characteristic contraction patterns upon exposure to caffeine and halothane plus caffeine. Patients who have never had a pyrexic reaction are designated as being MHS patients.

Patients who have drug-induced pyrexic crises have been recognized for some time as having myocardial involvement with necrosis and ventricular arrhythmias. Our patients demonstrate, in the absence of pyrexic crises, clinical, electrocardiographic, biochemical, hemodynamic and myocardial image changes consistent with myocardial involvement. Clinically, two of the four patients demonstrated musculoskeletal findings that had been previously described in patients with MH, i.e., strabismus and skeletal myopathy. Three of the four patients had abnormal ECGs, one with a long QT interval, one with significant Q waves and one with a right bundle and left anterior fascicular block pattern. At cardiac catheterization, all had normal coronary arteries but two had abnormal left ventricular wall motion and one had minimal mitral valve prolapse. Three patients had some elevation of serum CK and one patient had an elevation of CK-MB. Serum CK levels have been used as a screening test for MH susceptibility; however, it is possible for a patient who is susceptible to MH to have repetitive CK levels that are normal. Consequently, the test is only of value when it is elevated. Mitral valve prolapse has been described in association with ventricular arrhythmias but not in association with MHS. One of the four patients with a mid-systolic click and murmur had minimal mitral valve prolapse documented angiographically. The presence of prolapse in this patient may be a coincidental finding or related to abnormalities of the myocardium.

Ventricular arrhythmias have been described in patients having MH reactions after exposure to anesthetics. Spontaneous ventricular arrhythmias in MHS patients have not been recognized as part of the MHS clinical syndrome. In skeletal muscles, instability of membranes (sarcomplasmic reticulum) leads to abnormally high myoplasmic calcium levels. Similar instability of myocardial membranes would lead to abnormally high myoplasmic calcium levels and could produce electrical instability with ventricular arrhythmias as described in these patients. Two of the four patients had significant conduction system abnormalities, raising the possibility that specialized conduction cells are also involved in MHS.

The recognition of MHS is important because of the usual reaction of the skeletal and, possibly, myocardial cellular membranes to routinely used cardiac drugs, because of the effects of these drugs on calcium release.

Catecholamine-like vasopressors are contraindicated during an MH reaction even though the patient may be hypotensive. Use of these agents will lead to a mortality rate in excess of 90%. They may exert this deleterious effect on both skeletal and cardiac muscle by excessively activating adenyl cyclase. Catecholamines increase the influx of calcium into myocardial cells. The slow inward current, believed
to be carried primarily by calcium, is augmented. Catecholamines may also act by mobilizing calcium stores within the cell while also increasing the rate of calcium sequestration and speeding subsequent relaxation. Adenylate cyclase, a membrane bound enzyme which catalyzes the production of cyclic AMP from ATP in the presence of calcium, is activated by catecholamines which attach to $\beta$ receptors on the cell membrane. Catecholamines may act on the surface membrane of the cell to increase cyclic AMP, which may then effect changes in the release and uptake of calcium by the sarcoplasmic reticulum. The effect of $\beta$-adrenergic agonists may be mediated through their actions on cell membrane systems to affect the cyclic AMP system and hence calcium transport. In MHS patients these actions may produce excess intracellular calcium in both skeletal and cardiac muscle aggravating or even precipitating an MH reaction.

Cardiac glycosides accelerate calcium release from the sarcoplasmic reticulum in skeletal muscle, increase transfer of calcium from the intracellular to the extracellular state in cardiac muscle and increase death rates during MH reactions. Despite general agreement that cardiac glycosides affect the kinetics of the calcium involved in activating contraction, the specific nature of the events involved remains controversial. The cardiac glycosides have a very specific effect of binding to the surface membrane of the cardiac cells and reducing transsarcolemmal exchange of sodium and potassium. This is accompanied and presumably caused by the inhibition of the transport system which involves the sodium and potassium stimulated ATPase in the surface membrane with possible secondary effects on calcium. The inotropic effect of cardiac glycosides is accompanied by a net intracellular uptake of both sodium and calcium and a net loss of potassium. The accumulation of calcium within the cell, leading to augmentation of the intracellular calcium pool, may explain both the inotropic effects of glycosides and their adverse reactions in patients with MHS or MH reactions.

Certain drugs such as procaine or procainamide are beneficial in the treatment of MH reactions. These agents reverse rises of skeletal myoplasmic calcium by increasing influx into, and inhibiting release of calcium from, skeletal sarcoplasmic reticulum and may be beneficial in the treatment of patients with MHS with cardiac involvement. Unfortunately, other cardiac medications (table 4) used in the treatment of arrhythmias are known to be contraindicated in the treatment of MH reactions; for example, lidocaine. Its use significantly increases mortality in an MH reaction.

During the course of an MH reaction, rigidity is more apt to occur in patients who have had a belladonna alkaloid as premedication. The detrimental mode of action of this medication is not known. Calcium therapy is not recommended during an MH reaction even with hypocalcemia since, in skeletal muscle, exogenous calcium simply flows across the damaged sarcolemma into the interior of the cell, thus producing or aggravating muscle contracture. Finally, the production of elevated temperatures by quinidine in two of the four patients may have been coincidental or may represent an effect on the basic mechanism of the disease process. In view of known detrimental effects of the above medications during MH reactions and, because on rare occasions, these agents have been known to precipitate a hyperthermic reaction, their use would be contraindicated in MHS patients.

The presence of mitral valve prolapse in one patient and a prolonged QT interval syndrome in a second patient were limitations of this study. These syndromes are independently associated with ventricular tachycardia. Skeletal muscle biopsies are limited in number in such patients. Two additional patients with mitral valve prolapse and frequent unifocal ventricular premature beats (VPBs) volunteered for a skeletal muscle biopsy. Both of these patients had negative caffeine contracture studies. We have not yet had an opportunity to biopsy additional patients with the prolonged QT interval syndrome.

Since the completion of studies on these four patients, 12 additional patients with ventricular arrhythmias (multiform VPBs in seven, ventricular tachycardia in three, ventricular fibrillation in two), with known family histories of MH or family histories of sudden death (anesthetic and nonanesthetic-related), had had skeletal muscle biopsies. Eight of these 12 were positive on caffeine contracture testing (multiform VPBs in six, ventricular tachycardia in one, ventricular fibrillation in one). However, it must be emphasized that these patients represent a highly selected subgroup of patients with ventricular arrhythmias picked because of the strong suspicion of MHS. None of these additional 12 patients had mitral valve prolapse clinically or echocardiographically.

If MHS involves the heart, as suspected, then one can predict that a careful analysis of young patients with atypical chest pain, unexplained cardiomyopathies, a family history of sudden death, abnormal resting ECGs, myocardial infarct patterns with normal coronary arteries, unexpected abnormal elevations of CK or life threatening ventricular arrhythmias may lead to a diagnosis of MH.

**Table 4. Cardiovascular Medications that may Aggravate or Precipitate a Malignant Hyperthermic Reaction**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Amide type local anesthetics (lidocaine)</td>
<td></td>
</tr>
<tr>
<td>2) Belladonna alkaloids (atropine)</td>
<td></td>
</tr>
<tr>
<td>3) Calcium salts (gluconate and chloride)</td>
<td></td>
</tr>
<tr>
<td>4) Cardiac glycosides (digoxin)</td>
<td></td>
</tr>
<tr>
<td>5) Catecholamines</td>
<td></td>
</tr>
<tr>
<td>6) * quinidine</td>
<td></td>
</tr>
</tbody>
</table>

Medications in parentheses represent an example of each category.
Unexplained sudden death of a young person may warrant consideration of the diagnosis of MH with careful postmortem examination of skeletal and cardiac muscle histology. Conversely, careful evaluation of patients with previously diagnosed MH may lead to the recognition of cardiac involvement by the disease process.

We have presented four cases of MHS with a spectrum of cardiac involvement including atypical chest pain, abnormal ECGs, myocardial dysfunction and life threatening ventricular arrhythmias. The pathophysiologic mechanism may be a membrane defect leading to elevated myoplasmic calcium levels.

Acknowledgments

We greatly appreciate the technical assistance of Susan Physick, Jan Riddell and Sharon Umansky and the Department of Photography of the Toronto General Hospital.

References

33. Storesund A, Helle KB: Practolol, caffeine and calcium in the regulation of mechanical activity of the cardiac ventricle in myxine glutinosa (L.) Comp Biochem Physiol (C 52C): 17, 1975
35. Trautwein W: Membrane currents in cardiac muscle fibers. Physiol Rev 53: 793, 1973
42. Tsien RW, Giles W, Greengard P: Cyclic AMP mediates the effects of adrenaline on cardiac Purkinje fibers. Nature (New Biol) 240: 181, 1972
43. Nayler WG, Dunnett J, Sullivan A: Drug-induced changes in
the superficially located stores of calcium in heart sarcolemma. 
In Recent Advances in Studies on Cardiac Structure and
Metabolism, Vol 9, edited by Roy PE. Baltimore, University
Park Press, 1976, p 53
44. Glynn IM: The action of cardiac glycosides on ion movements.
Pharmacol Rev 16: 381, 1964
45. Lee KS, Klaus W: The subcellular basis for the mechanism
of inotropic action of cardiac glycosides. Pharmacol Rev 23: 193,
1971
46. Tada M, Kirchberger MA, Iorio JM, Katz AM: Control of card-
iac sarcomemal adenlylate cyclase and sodium potassium-acti-
vated adenosine triphosphate activities. Circ Res 36: 8, 1975
47. Langer GA, Serena SD: Effects of strophanthidin upon con-
traction and ionic exchange in rabbit ventricular myocardium:

Radiation Exposure to the Operator Performing Cardiac Angiography
With U-Arm Systems

STEPHEN BALTER, PH.D., F. MASON SONES, JR., M.D.,
AND RUSSELL BRANCATO, M.D.

SUMMARY We measured the radiation exposure received by a group of operators performing 700 coro-
mary angiograms. All studies were performed using the brachial artery approach and the Phillips Cardio
Diagnost. Nineteen sites were monitored on each operator, using lithium fluoride thermoluminescent
dosimeters. Four hundred examinations were performed with a table-mounted protective shield in place. Three
hundred were performed without the shield. The average exposures (in mR per study) with and without the
shield were 1.9/6 for the eyes and 1.4/8.3 for the thyroid.

The resulting operator exposure with the shield in place is low enough so that an operator performing 25
procedures per week on a continuous basis will not exceed the recommendations of the National Commission
on Radiological Protection and Units. We therefore strongly recommend the use of a properly designed and
appropriately positioned shield with all U-arm systems.

SEVERAL INVESTIGATORS HAVE STUDIED
the radiation doses received by physicians performing
the radiation doses received by angiographers include the
the lens of the eye and the thyroid (these organs are not
Shielded by the typical lead apron). Exposure of the
trunk is not as important with the universal use of

adequate lead aprons. Exposure of the extremities to
scattered radiation is of secondary importance due to
less radiation sensitivity in these areas.

Methods

Because of the wide differences in operator exposure
reported in the literature, we repeated the measurements under controlled conditions, with a
minimum number of variables. The clinical studies were all performed using a dedicated U-arm cardiac
angiography system (Phillips Cardio Diagnost). This
apparatus is shown in figure 1. The major variable was
the presence or absence of the table-mounted
operator's protective shield. This shield is shown in
place in figure 1. Figure 2 shows a close-up of the
shield before the application of sterile drapes. The sec-
ond significant variable was the nature of the medical
problems encountered and the nature of the manner in
which they were approached.

Further technical information on the apparatus and
its operation are given in table 1.

The experiment was divided into seven series of 100
consecutive adult examinations each. The first three
Cardiac manifestations of malignant hyperthermia susceptibility.
V F Huckell, H M Staniloff, B A Britt, M B Waxman and J E Morch

Circulation. 1978;58:916-925
doi: 10.1161/01.CIR.58.5.916

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1978 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://circ.ahajournals.org/content/58/5/916