Alterations in regional myocardial metabolism, perfusion, and wall motion in Duchenne muscular dystrophy studied by radionuclide imaging

JOSEPH K. PERLOFF, M.D., EBERHARD HENZE, M.D., AND HEINRICH R. SCHELBERT, M.D.

ABSTRACT  Studies at necropsy have shown that the cardiomyopathy of Duchenne muscular dystrophy selects the posterobasal and contiguous lateral left ventricular (LV) walls as initial and primary sites of myocardial dystrophy in the absence of small-vessel coronary artery disease in these areas. The present investigation was designed chiefly to determine whether a myocardial metabolic abnormality could be identified in these same areas during a patient's life. Positron emission computed tomography was used to study regional LV metabolism with \(^{18}F\) 2-fluorodeoxyglucose, and metabolism and/or perfusion was studied with \(^{13}N\)NH\(_3\). In addition, all subjects had the following performed: thallium-201 scans, technetium-99m multiple-gated equilibrium blood pool imaging, electrocardiograms, vectorcardiograms, and M mode and two-dimensional echocardiograms. \(^{18}F\) 2-fluorodeoxyglucose activity was selectively increased in the posterobasal and posterolateral walls of the left ventricle in 11 of 12 patients with technically adequate images, indicating accelerated regional exogenous glucose utilization. \(^{13}N\)NH\(_3\) activity was selectively decreased in the same areas in 13 of 15 patients, indicating either a regional metabolic alteration in uptake and trapping, a reduction in regional blood flow, or both. These data identify a myocardial metabolic abnormality concentrated in specific segments of the LV free wall in living patients with Duchenne dystrophy.


CLASSIC rapidly progressive Duchenne muscular dystrophy is X-linked recessive and is transmitted to male offspring by unaffected mothers.\(^1\) Population prevalence is approximately three per 100,000 with up to one-third of cases believed to be due to spontaneous mutations in either the patient or his mother.\(^1\) Histologic, ultrastructural, and serum enzymatic evidence indicate that Duchenne dystrophy exists from birth, and therefore in utero,\(^2\) although overt manifestations usually go unrecognized until the second year of life when the child begins to walk. Clinical detection of myocardial involvement was materially advanced by the electrocardiographic observations of Manning and Croop\(^3\) and Skyring and McKusick.\(^4\) Abnormal electrocardiograms (ECGs) are found even in early childhood.\(^5,6\) Tall right precordial R waves and increased R/S amplitude ratios together with deep Q waves in leads I, aVL, and V\(_{5,6}\) are characteristic of the classic rapidly progressive pseudohypertrophic X-linked dystrophy of Duchenne (figure 1).\(^3-12\) A reduction in or loss of electromotive forces caused by myocardial dystrophy in the posterobasal left ventricle (anterior shift of the QRS) and contiguous lateral wall (deep Q waves in leads I, aVL, and V\(_{5,6}\)) is believed to be the mechanism responsible for the characteristic ECG.\(^7-9,11\) Studies at necropsy showed that the above regions are the initial and most extensive sites of myocardial fibrosis,\(^8,10,11\) which is preceded by ultrastructural (subcellular) abnormalities.\(^11\) The primary posterobasal abnormality spreads to the epicardial third of the contiguous lateral left ventricular (LV) free wall with progressive transmural fibrous replacement.\(^11,13\) There is relative sparing of the ventricular septum and comparatively minimal involvement of right ventricular and atrial myocardium.\(^11,13\) Based on these observations, Duchenne dystrophy emerges as a unique form of heart disease characterized by a consistent and probably genetically determined predilection for specific regions of the heart — the posterobasal and lateral LV walls.\(^7-12\)
The present study was designed to ascertain whether metabolic, perfusion, or wall motion abnormalities could be identified in these areas in living subjects. To determine whether regional abnormalities of LV wall were present during life, noninvasive methods were required. Positron emission computed tomography (Positron-CT) using radioactive tracers for metabolism supplemented by thallium-201 (201TI) perfusion scans, gated equilibrium radionuclide angiography, and M mode and two-dimensional echocardiography provided these methods.

Materials and methods

The investigation included 15 patients, 6 to 24 years old (average 13.2), from the Carl M. Pearson Clinic for Neuromuscular Disease, University of California, Los Angeles. The criterion for admission into the study was a firm diagnosis of classic rapidly progressive X-linked Duchenne dystrophy based on clinical characteristics (consultant, Dr. David S. Campion, Director of the Clinic), together with serum enzymatic (creatine kinase), electromyographic and histologic (muscle biopsy) information. To quantify the degree of musculoskeletal disability, manual testing was done on all patients. The results were expressed as a percent of normal muscle function. The numerical value 5 signified full range of motion against gravity with strong resistance (100%); the numerical value 0 signified no visible or palpable contraction (0%). Scores under 40% indicated severe musculoskeletal disability.

Positron-CT was used to investigate regional myocardial utilization of exogenous glucose, and metabolism and/or perfusion was studied with 13NH3.22 No patient was taking medications that might have altered metabolism or perfusion. After an overnight fast, the subject was positioned in the UCLA whole body tomograph (ECAT II, Ortec Inc., Oak Ridge, TN).23 and transmission images were obtained for correction of photon attenuation. 13NH3 (10 to 15 μCi)21,22 was administered intravenously, and acquisition of four to five contiguous cross-sectional images of the heart spaced 1 cm apart was started 5 min after injection. Upon completion of image acquisition with 13NH3, the glucose analog 18F-2-fluoro 2-deoxyglucose (FDG) (5 to 10 μCi) was administered intravenously. After a 45 min wait to allow for decay of 13N activity (t½ = 9.9 min), clearance of FDG from the blood, and transport and phosphorylation of FDG in the myocardium,17-20 cross-sectional images of the regional myocardial FDG-6-phosphate concentrations were recorded at the same levels through the heart as for 13NH3. Identical patient positioning for both image sets was accomplished by carefully aligning the low-power neon laser beam of the tomograph with ink markers on the patient’s chest. Both image sets were analyzed visually by two independent observers for uniformity of myocardial 13N and 18F activity distributions. Studies were defined as abnormal when there were segmental increases or decreases in tracer concentrations and/or regional differences in the activity distribution between 13NH3 and the FDG images.

Production of FDG17 and 13NH3,22 as well as the performance characteristics of the Positron-CT,23 have been described previously. Imaging was performed in the low-resolution mode with a spatial resolution of 18 mm full-width half-maximum. Contiguous cross-sectional images were acquired in the decay-compensated mode so that the acquisition time per image increased in proportion to the physical decay of 13N (t½ = 9.9 min) or 18F (t½ = 109.8 min). As a result, the counts acquired were comparable for all images within one set and averaged 1,703,501 ± 430,283 for FDG and 1,611,079 ± 381,434 for 13NH3. The total acquisition time per image set was 20 min for 13NH3 and 60 min for FDG.

Regional myocardial perfusion in patients at rest was evaluated with intravenous 201Tl, and planar imaging was performed in the anterior and the 45 degree and 70 degree left anterior oblique projections with a gamma scintillation camera equipped with a high-resolution, low-energy, parallel-hole collimator. Resting LV function and wall motion were determined24 after intravenous administration of autologous red blood cells that were labeled in vitro with technetium-99m (99mTc), and after multiple ECG-gated equilibrium blood pool imaging was performed in the anterior, 45 degree left anterior oblique, and left lateral projections. Ejection fraction was calculated from the time activity curve derived from a variable region-of-interest assigned.
to the LV blood pool on each of the 16 background-corrected images. Regional wall motion was evaluated (visual inspection) by two independent observers.

A cardiac history was taken and a physical examination was performed for each patient. All patients had a 12-lead ECG, a vectorcardiogram (VCG) (Frank system), M mode and two-dimensional (Toshiba phased-array) echocardiograms performed, and determinations of total creatine kinase and its MB fraction were made.

The Positron-CT studies were interpreted blindly, i.e., by two observers who were unaware of the results of either the $^{201}$TI scintigrams, the $^{99m}$Tc equilibrium blood pool images, or the clinical findings. The ECGs, VCGs, and echocardiograms were interpreted without knowledge of the results of the radionuclide studies.

Results

Patients were divided into two groups based on their degree of musculoskeletal disability: (1) those with scores greater than 50% and (2) those with scores less than 50%. Four boys had scores of greater than 50%, were ambulant, and were 6 to 9 years of age. Eleven had scores of 50% or less, were in wheelchairs, and were 10 to 24 years of age. Total creatine kinase levels were elevated in all patients, ranging from 580 to 8500 U. The MB fraction was increased in two of 15, but not relative to total creatine kinase. The cardiovascular physical examination was normal in all patients except for frequent, intermittent, resting sinus tachycardia in 14 of 15. No patient had cardiac symptoms.

Results of radionuclide imaging are summarized in table 1 together with relative sensitivities of scintigraphic, Positron-CT, electrocardiographic, and vectorcardiographic findings. $^{13}$NH$_3$ uptake was decreased in the posterior, posterolateral, or inferolateral LV wall in 13 of 15, while 11 of 12 patients with technically adequate FDG images showed increased $^{18}$F activity in the same segments (figures 2 and 3). Three patients had little or no myocardial FDG uptake for reasons that were not established (plasma levels of free fatty acids, glucose, and lactic acid were normal). $^{201}$TI scintigrams disclosed mild reductions in perfusion of the posterobasal or lateral LV wall in three of 15 patients (figure 4). $^{99m}$Tc ventriculograms revealed LV ejection fractions of less than 50% in seven of 15 patients, and regional posterolateral, lateral, or inferolateral wall hypokinesis or akinesis in three of 15 (figure 5).

Standard ECGs (figure 1) showed increased right precordial R waves and increased R/S amplitude ratios in 13 of 15, abnormally deep Q waves in leads I, AVL, and V$_s$ in nine of 15 and abnormally deep Q waves in leads II, III, and aVF in one of 16. In no patient was the ECG entirely normal. The VCG exhibited an abnormal anterior shift of the QRS in 11 of 15, borderline anterior shift in two of 15, and no anterior shift in two of 15.

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<th>VCG $^{13}$NH$_3$</th>
<th>FDG</th>
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| Sensitivity | 20% | 27% | 40% | 80% | 87% | 92% | 100% |

RWMA = regional wall motion abnormalities; $^{201}$TI = myocardial perfusion at rest with $^{201}$TI scintigraphy; EF = left ventricular ejection fraction by equilibrium radionuclide angiography; $^{13}$NH$_3$ = N-13 ammonia; FDG = F-18 deoxyglucose images; + = abnormal study; NL = normal study; 0 = positron-CT study with no or insufficient FDG uptake.

$^a$The 92% sensitivity for the FDG images was derived only from the 12 patients with adequate myocardial tracer uptake.

M mode and two-dimensional echocardiograms were technically satisfactory in 14 of 15, revealing posterobasal LV wall motion abnormalities (hypokinesis) with mild thinning in three of 14. Mitral valve prolapse (moderate holosystolic hammocking) occurred in two patients (auscultation normal in both). Internal chamber dimensions were normal.

One patient (R.N., table 1) died at 17 years of age shortly after developing atrial flutter two years after study. At necropsy, the major myocardial involvement consisted of broad confluent, transmural, interlacing bands of fibrosis in the posterobasal and lateral LV walls. Normal appearing muscle cells (light microscopy) were found among these confluent bands of connective tissue. Minor foci of fibrosis were scattered in the epicardium of the inferior wall, septum, and right ventricular wall. Abnormalities of the coronary arteries, both extramural and intramural, were specifically sought but not identified.

Discussion

Metabolic and flow studies. The main objective of this investigation was to determine whether regional myocardial metabolic abnormalities could be identified.
During life in patients with Duchenne muscular dystrophy, and if so, whether the location(s) coincided with sites previously established as the primary areas of morphologic involvement at necropsy. In table 1, we report the sensitivity of FDG imaging for 12 of 15 patients in whom technically adequate studies were obtained. In 11 of 12 of these patients, accelerated exogenous glucose utilization in the posterobasal and contiguous lateral LV wall (figures 2 and 3) provides evidence of a regional myocardial metabolic abnormality. In 13 of 15 patients, $^{13}$N activity was reduced in the segments that exhibited increased $^{18}$F activity (figures 2 and 3). These are the same sites of primary dystrophic replacement found at necropsy.

Explanations for the observed regional increases in FDG concentrations are speculative. Segmental alterations in membrane permeability (see below) could be partially responsible. For example, the regional concentrations might be related to either an increase in distribution volume for FDG and glucose (i.e., a regional increase in transfer of glucose across capillary and cell membranes or a slower rate of back diffusion of glucose from tissue to blood) or a higher phosphorylation rate. Another possibility is an increase in the rate of phosphorylation perhaps due to the adenylyl cyclase abnormality identified in skeletal muscle with Duchenne dystrophy and (see below) or due to a compensatory increase in glycolysis in response to a decline in fatty acid oxidation. Perhaps relevant to the latter point are the observations on dilated cardiomyopathies in which Positron-CT with $^{13}$C-palmitate was used to detect decreased fatty acid utilization and marked spatial heterogeneity of accumulation together with large numbers of discrete, irregularly-shaped regions of depressed accumulation.

In three patients, myocardial FDG uptake was minimal, and clearance of $^{18}$F activity from blood was delayed, precluding adequate image analysis. It is unlikely that lack of myocardial FDG uptake signified far-advanced myocardial dystrophy because two patients had entirely normal LV function (wall motion) and only one had a globally depressed left ventricle.
and a regional perfusion defect by $^{201}$TI scintigraphy (table 1). In two of the three subjects, plasma free fatty acid concentrations were in the upper range of normal, while plasma levels of glucose and lactic acid were in the lower range of normal. Myocardial substrate utilization depends upon plasma substrate levels that also affect tracer uptake. In these two patients, absence of FDG might have been caused by preferential free fatty acid utilization with little uptake of glucose and, therefore, little uptake of FDG. In the third patient, free fatty acid levels were in the lower range of normal; if plasma insulin levels (not determined) were low, that might have accounted for the lack of glucose uptake, and hence, of FDG uptake. Alternatively, relatively small segmental increases in $^{18}$F activity in these three patients might have been obscured by residual $^{18}$F activity in blood due to delayed tracer clearance from the circulation.

Regional decreases in $^{13}$N activity in 12 of 15 patients (figures 2 and 3) could reflect a metabolic abnormality that reduced trapping, a regional decrease in flow, or both of these causes. Early in the natural history, i.e., in very young patients, it is reasonable to hypothesize that the high incidence of segmental reductions in $^{13}$N activity probably reflect altered regional myocardial metabolic uptake and trapping. Possible causes of the decreased trapping in affected myocardium are impairment of transmembrane tracer exchange or metabolic trapping per se. If alterations in myocardium with Duchenne dystrophy are analogous to those of skeletal muscle (see below), then a longer diffusion distance of an altered ionic milieu could result in decreased extraction fractions of $^{13}$NH$_3$. It is also possible that a regional depletion of the pool of glutamic acid, which binds the tracer in tissue, contributes to segmental reduction in $^{13}$NH$_3$. However, regional perfusion defects do occur, as demonstrated by thallium scintigraphy in four of our patients (table 1), and at those stages in the natural history, decreased perfusion could reasonably be considered one determinant of segmental reductions in $^{13}$NH$_3$ activity. To this point, $^{13}$NH$_3$ as a tracer of blood flow has been demonstrated in canine myocardium over a wide range of hemodynamic and metabolic alterations induced over the short term but not over the long term. We believe that the mechanism(s) governing regional reductions in myocardial blood flow in Duchenne dystrophy probably relate to a decrease in myofibers per unit mass.

**FIGURE 3.** Regional myocardial $^{13}$NH$_3$ (A) and FDG (B) uptake visualized in three contiguous Positron-CT images of the left ventricular myocardium in patient M.B., also shown in figures 4 and 5. There is a segmental decrease in $^{13}$N activity in the posterolateral wall (arrows) with a discordant increase in FDG concentrations in the same segment (arrows). This patient had a moderate posterolateral $^{201}$TI defect, posterolateral akinesis, and a left ventricular ejection fraction of 46%.
FIGURE 4. Rest $^{201}$Tl scintigrams recorded in the anterior (ANT), 45 degree left anterior oblique (LAO), and 70 degree lateral (LAT) projections in two patients. In patient A (R.N.), the myocardial perfusion images were normal. By contrast, the images of patient B (M.B.) revealed a moderate decrease in $^{201}$Tl activity in the posterolateral wall indicated by the arrows in the LAO and LAT projections.

FIGURE 5. Equilibrium radionuclide angiograms in the same two patients shown in figure 4. The end-diastolic (ED) and end-systolic (ES) frames in the anterior (ANT) and the 45 degree left anterior oblique (LAO) projections are shown. The left ventricular cavity silhouettes in ED and ES are superimposed on the right. In patient A (R.N.), wall motion is concentric and of normal amplitude with an LV ejection fraction of 55%. In patient B (M.B.), there is akinesis of the posterolateral wall seen best in the LAO projection (arrow). The ejection fraction in this patient was 46% (Ao = ascending aorta; RA = right atrium; RV = right ventricle).
(fibrous replacement) and/or to an increase in the number of intrinsically injured but viable posterobasal and lateral LV myocardial cells that might require less oxygen and, accordingly, less flow. Earlier studies together with the study at necropsy in this report identified no luminal narrowing (light microscopy) of either extramural or intramural coronary arteries in the involved segments.

We cannot draw conclusions on whether the segmental variations in ammonia concentrations observed in our studies were primarily related to cell membrane changes, to changes in myocardial cell metabolism, or to changes in blood flow. However, data on skeletal muscle in Duchenne dystrophy (see below) prompt us to hypothesize that the regional myocardial abnormalities of both FDG and $^{13}$NH$_3$ represent secondary metabolic alterations initiated by a basic defect in cardiac plasma cell membrane.

Despite intensive investigation and a number of major advances, the basic pathogenetic defect in Duchenne dystrophy remains elusive. Early evidence that abnormalities of striated muscle blood flow were responsible for some forms of experimental muscular dystrophy$^{35}$ have not been confirmed in patients with Duchenne dystrophy by the use of the local $^{133}$Xe injection method at rest and during hyperemia, supplemented by the capacity of capillary diffusion measured with the $^{51}$Cr-EDTA.$^{36}$ Furthermore, electron microscopic and morphometric studies of the microvasculature in skeletal muscle of Duchenne dystrophy provide no evidence that dystrophic changes are caused by a primary abnormality of muscle microcirculation.$^{37}$

Current evidence — both ultrastructural and biochemical — supports the hypothesis that the basic abnormality in Duchenne dystrophy resides in plasma cell membranes, not only in those of striated muscle fibers (figure 6),$^{27, 38-47}$ but also in those of red blood cells,$^{48, 49}$ and probably in those of fibroblasts.$^{48, 50}$ Initial, localized, structural lesions in the sarcolemma are followed by (and are responsible for) muscle fiber degeneration and abnormalities of organelles within the fiber.$^{41, 45-47}$ Ultrastructural changes in the plasma membrane vary from focal rarefaction to total absence.$^{45-47}$ Plasma membrane was absent on part or all of the circumference of muscle fibers at biopsy from infants and children as young as 9 months to 3 years of age, and in fibers varying from morphologically normal to clearly necrotic.$^{47}$ Highly contracted myofibrils border the zones of focal plasma membrane rarefaction as if in response to uncontrolled entry of calcium-rich extracellular fluid into the myofibrillar space.$^{41, 45, 47, 51}$ Focal ultrastructural defects of the surface membrane apparently offer an ineffective barrier to the ingress of extracellular fluid (as evidenced by entrance of peroxidase containing fluid into the fiber interior)$^{45}$ and contribute to leakage of cytoplasmic enzymes that are typically and markedly elevated.$^{52}$ The plasma membrane is therefore believed to be the basic vulnerable organelle in Duchenne dystrophy and is held responsible for initiating the dystrophic process by permitting entry of extracellular fluid into the muscle fiber, changing its ionic milieu, and adversely effecting myofibrils as well as other organelles (figure 6).

In addition to the ultrastructural abnormalities described above, it has been argued that, as in other genetic diseases, there must be a biochemical fault.$^{53}$ A number of lines of evidence point to the surface membranes of skeletal muscle as being not only structurally affected, but also biochemically affected.$^{26, 27, 40, 43, 46, 47}$ Studies of Duchenne dystrophy muscle cells in culture permit isolation of sarcolemma from muscle fiber and indicate that abnormal enzyme activity (adenyl cyclase) occurs as early as the miotube stage of development.$^{26}$ Comparative studies of $^{31}$P nuclear magnetic resonance profiles of intact normal and diseased skeletal muscle disclosed a conspicuous absence of glycer-
ol 3-phosphorylcholine (GPC) in Duchenne dystrophy.\(^4^3\) Because GPC is a derivative of lecithin, a constituent of muscle membranes, alterations in GPC metabolism were believed to reflect changes in the membranes of dystrophic cells.\(^4^3\) Early focal defects in concanavalin A (Con A) binding on muscle cell surfaces were noted even in the presence of intact plasma membrane and normal subsurface intracellular structures, implying that a biochemical abnormality of the cell membrane preceded the morphologic changes of membrane or subsarcolemmal structures.\(^4^6\) Importantly, Con A binds specifically to certain carbohydrate residues, namely, \(\alpha\)-D-mannose, \(\alpha\)-D-glucose, and \(\alpha\)-D-fructose,\(^4^6\) but whether this observation is related to the abnormal uptake of FDG in our patients is unknown. Interestingly, impaired glucose tolerance or abnormal carbohydrate metabolism have not been identified in Duchenne dystrophy.\(^5^4,\,5^5\) although decreased insulin binding to monocytes (low insulin receptor concentration) has been documented.\(^5^5\)

A relationship between published observations on skeletal muscle with Duchenne dystrophy and our observations on cardiac muscle is important but presently speculative. Data on skeletal muscle suggest by analogy that a primary abnormality of regional blood flow is not pathogenetically important in myocardial dystrophy. Electron microscopic studies of myocardium with Duchenne dystrophy are necessarily few, since biopsy specimens cannot safely be secured from selective sites in the posterolateral wall of the LV. A study of two hearts removed 1 to 3 hr after death disclosed ultrastructural changes that were believed to be identical to those of skeletal muscle with Duchenne dystrophy.\(^7^1\) Not surprisingly, late-stage specimens showed extensive myofibrillar loss, but oddly, only rare sarcocelmal changes. Taken at face value, these authors\(^7^1\) purport that abnormalities of skeletal muscle plasma membrane in Duchenne dystrophy are rare, a conclusion at variance with the other data cited above.

**Electrocardiographic and vectorcardiographic studies.** With a single exception, the anterior shift of the QRS and the lateral wall Q waves (leads I, aVL, and V\(_{5,6}\)) coincided with abnormalities of FDG and of \(^{13}\)NH\(_3\) concentrations in the posterobasal and lateral LV walls. In one 14-year-old patient, there were posterolateral abnormalities of \(^{13}\)NH\(_3\) and FDG uptake, but the ECG showed only abnormally deep Q waves in left precordial leads with no significant anterior shift of the QRS on either the ECG or VCG. If a reduction in or loss of posterolateral LV electrical forces is in fact the cause of the distinctive ECG in Duchenne dystrophy,\(^7,\,9,\,1^1\) this loss of forces apparently does not require transmural replacement of myocardium by inert connective tissue. Increased FDG concentrations in these areas, together with normal regional wall motion in nine of 15 patients, are consistent with either the presence of abnormal but viable (metabolically active) contracting myofibers or preservation of a sufficient population of normal myofibers.

**LV wall motion studies.** LV ejection fractions determined by gated equilibrium radionuclide angiography were reduced 40% to 50%, mean 44.6%) in six patients. It is unlikely that these abnormalities were due to deconditioning.\(^5^6\) LV internal dimensions were normal in these six subjects, but the two with the lowest ejection fractions (40% to 44%) exhibited global decreases in free wall motion. Since abnormalities confined to the posterolateral wall should not cause global depressions of LV function or reduced ejection fractions, these observations imply that otherwise occult disease had spread to most if not all of the free LV wall.\(^1^1,\,1^3\) Regional hypokinesis or akinesis of the posterolateral wall was found in three of nine other patients (figure 5), two of whom had no identifiable abnormalities of wall motion by echocardiography. Conversely, a regional wall motion abnormality found by echocardiography in one patient was not identified on the gated blood pool scan. Regional decreases in mean systolic and diastolic endocardial velocity and wall motion at echocardiography have been reported by others.\(^1^5,\,5^7,\,5^8\) Taken together, radionuclide angiography and echocardiography detected segmental abnormalities of the posterior or posterolateral LV wall in four patients and global decreases in wall motion in two.

**Important unanswered questions.** Do the observed alterations in regional LV uptakes of FDG and \(^{13}\)NH\(_3\) represent metabolic abnormalities initiated by a primary defect in plasma cell membrane analogous to, if not identical with, that proposed for skeletal muscle in Duchenne dystrophy (figure 6)? These segmental LV abnormalities of FDG and \(^{13}\)NH\(_3\) concentrations may represent the first step in revealing the cardiomyopathy of Duchenne dystrophy as a unique form of heart disease that targets a specific region of LV wall as the primary site of a genetically determined biochemical abnormality. Fresh biopsy specimens from skeletal muscle are readily accessible for biochemical and ultrastructural analyses,\(^5^9\) but regional LV myocardial biopsy specimens will, in the foreseeable future, remain unavailable. Accordingly, refined methods of myocardial imaging will continue to play major roles in investigating the hearts of living subjects with Duchenne dystrophy. Nuclear magnetic resonance has been used
to study the metabolism of intact normal and diseased skeletal muscle, 43, 60 but for the predictable future, Positron-CT promises to maintain its importance in the study of metabolism of the intact myocardium. We are presently extending Positron-CT to include 11C-palmitate in an effort to determine whether the observed increases in regional concentrations of FDG in hearts with Duchenne dystrophy might be due to a compensatory increase in glycolysis in response to a decline in fatty acid metabolism. Radiolabeled amino acids will be used in an attempt to shed light on the possibility that an abnormality of amino acid metabolism might accompany the regional decreases in 13N activity. In addition, we are applying Positron-CT (FDG, 13NH3, and 11C-palmitate) to study the posterolateral LV wall in female carriers. Irrespective of technique, an important objective remains the study in vivo of the myocardial plasma cell membrane in Duchenne dystrophy apart from and in addition to the myofiber.

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Erratum

Line 5 of the abstract should read as follows: “All patients had a comparable follow-up time of approximately 23 months, which showed that cumulative thromboembolic rates were significantly lower after St. Jude valve implantation than after Björk-Shiley valve implantation.” The following sentence should have appeared immediately thereafter: “Postoperative event-free rates for all complications were significantly higher for the patients with St. Jude aortic valves (up to 48 months) and with St. Jude mitral valves (up to 52 months) than for patients with Björk-Shiley implants.”
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Circulation. 1984;69:33-42
doi: 10.1161/01.CIR.69.1.33

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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