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Cardiovascular Research 33 (1997) 13–22

Cardiovascular Research

Review

Cardiac disease in myotonic dystrophy

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Received 5 January 1996; accepted 6 June 1996

Abstract

Cardiac disease is a well-known complication of myotonic dystrophy, understanding of which has been increased by recent advances in both molecular techniques and cardiological investigations. Conduction disturbances and tachyarrhythmias occur commonly in myotonic dystrophy. These have been shown to have a broad correlation in severity with both neuromuscular disease and the extent of the molecular defect in some, but not all, studies. Clinical evidence of generalised cardiomyopathy is unusual. The rate of progression differs widely between individuals; sudden death may be caused by ventricular arrhythmias or complete heart block, and this can be at an early stage of disease. A familial tendency towards cardiac complications has been shown in some studies. The histopathology is of fibrosis, primarily in the conducting system and sino-atrial node, myocyte hypertrophy and fatty infiltration. Electron microscopy shows prominent I-bands and myofibrillar degeneration. Myotonin protein kinase, the primary product of the myotonic dystrophy gene, may be located at the intercalated discs and have a different isoform in cardiac tissue. The role of other genes or the normal myotonic dystrophy allele in myotonic heart disease has yet to be determined. Suggestions for clinical management include a careful cardiac history and a 12-lead ECG at least every year, with a low threshold for use of 24 h Holter monitoring. Extra care should be taken before, during and after general anaesthetics, which carry a high frequency of cardiorespiratory complications. Finally, myotonic dystrophy should be considered in previously undiagnosed patients presenting to a cardiologist or general physician with suspected arrhythmia or conduction block.

Keywords: Myotonic dystrophy; Myotonin protein kinase; Tachycardia; Arrhythmias; Conduction

1. Introduction

Myotonic dystrophy (dystrophia myotonica, Steinert's disease), the commonest muscular dystrophy of adult life, is a multisystem disorder with a prevalence of 1 in 8000. Delineation as a distinct disorder was by Steinert in 1909 [1] and it was this very first paper that suggested cardiovascular involvement, as bradycardia was noted to be a feature of several cases. Knowledge of the molecular basis of myotonic dystrophy has also advanced, with the discovery in 1992 of the myotonin protein kinase gene at 19q13.3, which contains an unstable CTG trinucleotide repeat [2–4]. There are several reviews available of myotonic dystrophy as a whole [5,6]. There are three broad forms of myotonic dystrophy: congenital, classical and minimal, all of which may occur in the same kindred. Congenital myotonic dystrophy is symptomatic at birth or in the first year of life, presenting with some or all of: respiratory and feeding difficulties, maternal polyhydramnios, developmental delay and talipes equinovarus. Later many of the symptoms and signs of classical myotonic dystrophy occur. This form is almost always maternally transmitted. Myotonic dystrophy can also start during childhood and it then follows a pattern similar to a more severe form of classical myotonic dystrophy.

Classical myotonic dystrophy has its onset between 10 and 60 years, presenting with: myotonia; muscle weakness in a classical distribution of facial, temporalis, sternomastoid, and distal limb muscles; cataracts; smooth muscle and cardiac muscle involvement; and somnolence.

Minimal myotonic dystrophy has its onset after 50 years, only manifesting cataracts, myotonia and a mild degree of muscle weakness. Some individuals with minimal myotonic dystrophy only have cataracts with no neuromuscular abnormalities present.

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PII S0008-6363(96)00163-0

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Knowledge concerning cardiac disease in myotonic dystrophy has progressed in tandem with developments in cardiological investigation. Conduction defects were shown to be common by Evans in 1944 [7]. In 1967 Church reviewed 300 cases from the literature and 17 cases seen prospectively [8]. The conclusion was that patients are rarely symptomatic, but if so this was usually due to arrhythmia. In contrast, many asymptomatic patients showed ECG changes, usually conduction disturbances. Cardiac disease bore no relationship to neurological disease, and pathology by light microscopy was non-specific.

Over the last 25 years there has been more detailed exploration of these basic findings. This review gives a summary of such advances and is organised as follows:

1. Molecular advances and clinical genetic studies.
2. Cardiac pathology.
3. Clinical manifestations: (a) Conduction delay. (b) Rhythm disturbance. (c) Myocardial disease.
4. Management and clinical presentation.

Many cardiac studies have not distinguished between the different forms of myotonic dystrophy in the patients investigated, but, probably because it is the commonest form to come to medical attention, classical myotonic dystrophy represents the majority of cases in such studies. However, many of the studies which will be quoted do include cases of congenital and minimal myotonic dystrophy, or have not explicitly stated that only classical patients were studied.

2. Molecular advances and clinical genetic studies

Isolation of the myotonic dystrophy gene has given the first possibility of understanding the primary defect and of relating this to the cardiac and neuromuscular pathology seen in the disease.

The specific mutation underlying myotonic dystrophy is an unusual one, belonging to the newly recognised category of unstable trinucleotide repeats. The trinucleotide repeat in myotonic dystrophy is situated in a non-coding region of the DMK (myotonin protein kinase) gene and so would be expected to produce any pathological effects by influencing transcription or translation rather than by causing a change in the primary structure of the protein. It is also possible that the expanded repeat affects the structure of adjacent genes. Further study of myotonin protein kinase has given some conflicting results, but a pattern is emerging as regards its localisation and the probability of differing isoforms. Several groups have raised antibodies against differing domains of the protein. One common finding is localisation of the protein by immunostaining to the intercalated disc regions of cardiac muscle [9–12]. There are differing findings on the size of the protein, which may be a result of different methodological approaches. Suggestion of a different isoform in cardiac tissue has been reported [10,11,13]. No change and decreased levels [12,13] of protein in myotonic dystrophy have been reported. Concerning cardiac disease, this has been correlated with the length of the CTG triplet repeat, with differing results. An investigation of 14 patients showed no such correlation [14]; another, which divided 42 patients into 3 subgroups according to triplet repeat length [15], did show a correlation in that the incidence of normal ECG findings was inversely proportional and the incidence of left bundle branch block, of abnormal ventricular late potentials and of ventricular triplets and couplets was directly proportional to the expanded triplet repeat size. As both groups mention, somatic heterogeneity in the length of the CTG expansion [16,17] may make interpretation of results difficult if expansion size in blood lymphocytes is used when comparing with cardiac disease. Another confounding factor may be that patients with larger repeat sizes may have had symptomatic disease for longer than those with smaller repeats when cardiac investigations are carried out and so this needs to be accounted for.

There is evidence that myotonic heart disease is more common in certain families. A study of 18 families showed 4 to have at least 2 members with conduction abnormalities or arrhythmia and 14 families to have no members with these defects [18]. None of the unaffected relatives had arrhythmia or conduction block. There have also been case reports of families with myotonic heart disease and this is in the absence of ischaemic heart disease or diabetes mellitus [19,20,21,28].

A recent important finding is of a second gene immediately adjacent whose function could be affected by the expansion in the myotonin protein kinase gene [22]. The role of the gene for progressive familial heart block type 1 (PF-HB1) may also be significant. This has been mapped to 19q13.2-13.3, close to the myotonic dystrophy locus [23]. Individuals affected by PF-HB1 suffer a similar range of cardiac complications to those with myotonic dystrophy. It has been postulated that the myotonic dystrophy triplet repeat expansion may interfere with gene expression at the PF-HB1 locus, resulting in the cardiac conduction disturbances seen in myotonic dystrophy, though there is no direct evidence for this yet [23].

Cardiac repair mechanisms are influenced by the angiotensin-converting enzyme genotype [24,25] and it may be that certain genotypes influence the progression of myotonic heart disease, but no studies have been published on this. Therefore, there are several ways in which myotonic heart disease could have a familial pattern: it may relate to a change in the function of DMK itself; to the influence of other nearby genes because of a direct effect of the abnormal CTG repeat; to differences in the ability to repair cardiac tissue; it may also be connected with the function of the normal allele in a person with myotonic dystrophy.

It is clear that much further study of the primary biochemical defect will be needed to resolve the situation.

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3. Cardiac pathology

Although the cause of the pathological process in cardiac disease is not known yet, the resultant histological changes are (Table 1). These are not always seen on light microscopy, but when present the most constant findings are myocyte hypertrophy, interstitial fibrosis and fatty infiltration [26–29]. A few cases also show myofibre disarray and infiltration of lymphocytes. The distribution of myocardial fibrosis differs and has been noted to be predominantly perivascular but also pericellular and patchy.

On electron microscopy there are more specific changes of myofibrillar degeneration and prominent I-bands, with some specimens also having abnormal mitochondria.

In 1972 Rausing [21] described 3 cases of focal myocarditis in a family. The pathology was that of an acute myocarditis that could not be ascribed to another cause in 2 out of the 3 cases. Other studies have also seen clusters of lymphocytes [27]; it has been suggested that some of the fibrosis and fatty infiltration usually seen follows a silent acute myocarditis, but there is little evidence to support this.

A study of 12 patients by Nguyen et al. [27] showed that the predominant lesions in the conducting system were fibrosis of the sinus node, atrioventricular node and the left bundle branch, also fatty infiltration of the His bundle. On correlating the lesions with ECG abnormalities fibrosis was seen in the corresponding sections of the conducting system but was also seen where there was no ECG abnormality. This may reflect the inadequacy of ECG recordings in showing minor abnormalities in the conducting system. Inevitably there have not been many cases studied in detail by both electrophysiology and histopathology.

A possible link between histological (and thus clinicopathological) features and the molecular defect is an abnormality in myocardial glucose metabolism. A study of myocardial glucose utilisation in adults with myotonic dystrophy [30] has shown reductions in the myocardial metabolic rate for glucose (MMRGlu) and in glucose phosphorylation rate ($k3$) between subject and controls in the absence of a difference in myocardial bloodflow, myocardial capillary areas, decreased substrate availability or decreased blood–tissue transfer rate, leaving a primary abnormality of glucose utilisation in cardiac tissues as an explanation. MMRGlu and $k3$ were also found to be inversely correlated to CTG expansion size. The impaired protein in myotonic dystrophy is a serine-threonine protein kinase, and an alteration in its function may thus be linked to such observations of decreased glucose utilisation and phosphorylation.

Table 1
Light and electron microscopy findings in cardiac muscle

Findings	Histology of cardiac disease in myotonic dystrophy	
	Most frequent	Occasional
Light microscopy	Myocyte hypertrophy Fatty infiltration Interstitial fibrosis	Myofibre disarray Infiltration of lymphocytes
Electron microscopy	Myofibrillar degeneration Prominent I bands	Abnormal mitochondria

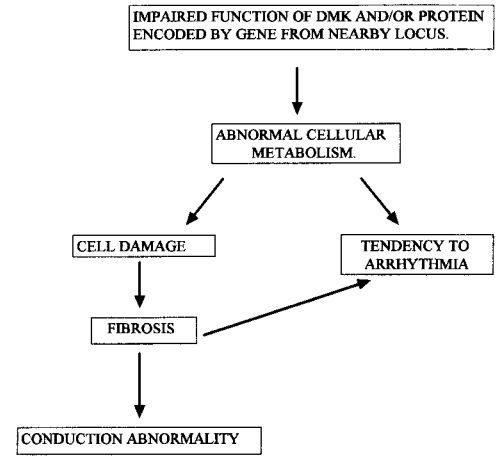

Fig. 1. Flow chart of possible origin of conduction and rhythm disturbances in myotonic dystrophy. The impaired protein function may lead to abnormal cellular metabolism, which may cause cell damage and alter the ionic flux across the cell membrane. Both of these may increase the tendency to arrhythmia and fibrosis resulting from cell damage can lead to conduction abnormalities.

Taking these facts into consideration, a possible scenario for the various manifestations of cardiac disease in myotonic dystrophy could be as in Fig. 1.

4. Clinical manifestations and presentation

The basic findings of conduction disturbance and arrhythmia summarised by Church [8] in 1967 still hold true, with cardiomyopathy being much less common—it has been suggested that there is no cardiomyopathy in myotonic dystrophy. Patients are often asymptomatic, and the true incidence of cardiac disease in myotonic dystrophy is uncertain both because of this and because only a few studies have investigated patients unselected for cardiac symptoms or disease [15,31–34,41]. The overall incidence of ECG abnormalities in these studies ranged from 37 to 80%.

4.1. Conduction delay

Any section of the conducting system can be affected, but it is the His-Purkinje system which is primarily involved. The evidence for this is prolongation of the PR interval, QRS duration and HV (His bundle to ventricle) interval, as well as histological changes. The main clinical concern is the development of complete heart block and the role of this in sudden death. Left and right bundle branch block are seen in approximately equal numbers,

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varying from 5 to 25% [8,15,27,29,31,32,34–38]. The HV interval was increased in 56% of cases [34] in one study that did not specifically investigate patients with known cardiac abnormalities and the PR interval in 21 to 40% [8,15,27,29,31–33,35–39,41]. Table 2 shows abnormalities in conduction as shown in several studies—this is not a comprehensive list, but serves to illustrate the variation found between different studies. A lot of this is because of using different patient groups as studies vary in the classes of DM, in numbers studied, in age range, in known cardiac abnormalities studied, and not all specify such factors. Of the studies shown in the table only the one by Fragola et al. [35] specifically stated that all patients were unselected for cardiac disease and had classical myotonic dystrophy.

From a clinical viewpoint it is important to know the rate of change of conduction system abnormalities. Studies on this are conflicting to some extent, but this may represent differences in the length of follow-up and in disease severity [31,35,39,40]. Table 3 compares these 4 studies with the general consensus being that there is a gradual, and very occasionally rapid, progression of conduction system disease, but the rate of this progression cannot, as yet, be predicted in an individual patient.

Sinus bradycardia has been noted in 5 to 25% of patients in most series [15,27,29,32,35,36,41], and this is often in conjunction with other abnormalities such as abnormal sinus node function and various degrees of heart block.

4.2. Rhythm disturbance

Most types of tachyarrhythmia have been described (Table 4), the comments applied to Table 2 being relevant again here. Atrial flutter and fibrillation are the commonest, being found in up to 25% of patients [8,27,29,31,32,35,38,38], and in most studies. There have been no studies on ventricular rate, use of anticoagulants or drug treatment of atrial fibrillation. Ventricular arrhythmias have most often been reported in single case studies [26,42–44] or as short episodes in studies using 24 h ambulatory electrocardiography [27,32,36,38]. They represent a major problem in management.

Correlation of neuromuscular disease with severity of cardiovascular disease will be affected by this varying progression of cardiac disease between individuals and also by the different ways in which this can be measured (e.g., as presence of any ECG abnormality, or the number or degree of cardiac abnormalities). These factors may partly explain the difference between studies investigating this correlation: no relationship [32,35,39,41], an increase in abnormalities [35], or positive correlation with abnormal CTG repeat length [15] (which itself correlates with severity of neuromuscular disease) have all been reported. Overall it appears that in mild neuromuscular disease lesser degrees of cardiac involvement, such as first-degree heart block, may be present whereas in more severe neuromuscular disease there are often additional abnormalities, with higher degrees of conduction block and arrhythmias.

4.3. Myocardial disease

Overt clinical symptoms of myocardial disease are rare. This may be because of the reduced level of activity in myotonic dystrophy as well as diffidence in reporting symptoms, or it could be because cardiomyopathy is actually very rare.

A few cases of biventricular failure have been reported [45,46] in the absence of arrhythmia, but it is difficult to judge whether this is cardiomyopathy coincidental with myotonic dystrophy or actually due to the disorder itself. The question of whether there is subclinical myocardial dysfunction has been addressed in several studies [31,35,38,47,48]. On ECG there are often abnormal Q-waves and ST segments in the absence of coronary artery disease. Echocardiography reveals mitral valve prolapse in 25–40% of most series [15,32,36,38]. The mitral valve prolapse is thought to be related to papillary muscle dysfunction and is not associated with arrhythmias.

Table 2
Conduction abnormalities and symptoms in myotonic dystrophy

Study	Symptoms	PR prolonged	LBBB	RBBB	LAD	LFB	ST/T-wave abnormal	QT prolonged
Hawley et al. [31] [a]	–	16/37	3/37	2/37	–	6/37	–	–
Komajda et al. [37]	4–faintness 3–syncope	8/12	4/12	3/12	1/12	0/12	–	–
Oloffson et al. [34] [a]	Not commented on	13/63	3/63	3/63	–	12/63	17/63	3/63
Pencic-Popovic et al. [36]	Not commented on	1/20	0/20	0/20	–	2/20	11/20	4/20
Nguyen et al. [27]	5–palpitations	6/12	3/12	2/12	3/12	–	–	–
Fragola et al. [35] [a,b]	Not commented on	23/56	5/56	9/56	–	9/56	–	–
Hiromasa et al. [38]	3–palpitations	8/10	2/10	0/10	–	6/10	–	–
Melacini et al. [15] [a]	3–presyncope	12/42	6/42	7/42	–	8/42	–	–
Motta et al. [29]	2–palpitations	2/8	1/8	1/8	–	–	–	–

[a] Study where patients were not preselected for cardiac disease or symptoms. [b] In this study 12-lead ECG and 24 h ECG findings were shown together; in this table those identified as 'intermittent' in the original paper are also included. PR prolonged = criteria given differed between papers; LBBB and RBBB = left and right bundle branch block, respectively; LAD = left axis deviation; LFB = left fascicular block; QT_c prolonged = criteria differed between papers.

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Table 3
Progression of conduction system disease as studied in 4 papers

Study	No. of subjects	Mean period of follow-up (months)	Initial conduction disturbances	Final conduction disturbances	Comments
Florek et al. [39]	45	54	17(38%) had a conduction abnormality	62% had a conduction abnormality	
Prystowsky et al. [40]	9	35	7 with first-degree block, 3 of which had HVI > 55 ms, 1 with LBBB	Same 7 with first-degree block, 7 had HVI > 55 ms	Initial HVI did not predict conduction disease progression
Fragola et al. [35]	56	52	16 with first-degree block, 2 with BBB, 3 with hemiblock, 1 with pacemaker	14 developed additional degrees of block, 6 had first appearance of conduction system disease, 9 with pacemakers.	No certain way to predict appearance or progression of conduction system disease
Hawley et al. [31]	31 (7 with congenital myotonic dystrophy)	72	1 with BBB, 2 with LAH, 9 with first-degree block	6–new appearance of BBB, 1 with LAH developed BBB, 10–first degree block	Increase in PR interval in all but 3. All progression of conduction system disease was gradual

BBB = bundle branch block; LAH = left anterior hemiblock; HVI = His to ventricle interval.

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Table 4
Arrhythmias as shown on standard 12-lead ECG and 24 h tape

	12-lead ECG						24 h tape			
	Symptoms	Atrial flutter/ fibrillation	Ventricular tachycardia	Pacemaker	Sudden death	Premature ventricular contractions	Atrial flutter/ fibrillation	Supraventricular tachycardia	Ventricular tachycardia	Premature ventricular contractions
Hawley et al. [31] *	—	2/37	—	1/37	1/37	—	—	—	—	—
Komajda et al. [37]	4 had symptoms of faintness, 3 syncope	2/12	0/12	0/8	—	—	—	—	—	—
Rakovic et al. [41] *	5 had palpitations	0/8	0/8	—	0/8	0/8	0/8	0/8	0/8	0/8
Olofsson et al. [41] *	Not commented on	7/65	—	2/65	—	—	—	—	—	—
Pencic-Popovic et al. [36]	Not commented on	0/20	0/20	—	—	1/20	0/20	6/20	0/20	17/20
Nguyen et al. [27]	5 had palpitations	2/12	3/12	—	3/12	1/12	—	—	—	—
Fragola et al. [35] *,#	Not commented on	1/56	2/56	10/56	1/56	—	7/56	2/56	—	4/56
Perloff et al. [32] *	5 had palpitations, 2 lightheadedness	—	—	1/25	—	—	1/25	1/25	1/25	9/25
Hiromasa et al. [38]	3 palpitations	0/10	2/10	0/10	—	3/10	3/10	0/10	2/10	2/10
Melacini et al. [15] *	3 presyncope	0/42	—	2/42	—	—	0/32	0/32	0/32	3/32
Motta et al. [29]	2 had palpitations	1/8	0/8	0/8	0/8	0/8	1/8	0/8	0/8	2/8

* Study where patients were not selected for cardiac disease or symptoms.

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Radionuclide angiography studies have been applied to measure cardiac performance during exercise [42,49,53] and these have shown a subnormal left ventricular ejection fraction response to exercise in some patients. However, this measurement reflects the whole cardiovascular response to exercise and is thus dependent on other factors such as muscle blood flow, central control and heart rate. A more recent study [48] used load-independent indices of left ventricular function by calculating left ventricular end-systolic stress. This found no difference between myotonic dystrophy patients and controls, no difference between patients with mild and moderate/severe neurological disease and no difference between patients with and without conduction disturbances.

Investigation of the role of possible myocardial myotonia has been more limited [50,51]. The study by Child and Perloff measured the rate of early relaxation of the posterior left ventricular wall, defining this as diastolic endocardial velocity maximum (DEVM). Ten of 20 patients (drawn from a clinic for neuromuscular diseases) showed a significant prolongation of DEVM. This group also had longer mitral deceleration times and isovolumetric relaxation times. These results suggest delayed myocardial relaxation. This study also found no difference in left ventricular size, fractional shortening or ejection fraction between subjects and controls [51].

5. Management and presentation of cardiac disease

From what has already been discussed it is clear that management of myotonic heart disease is a difficult problem. The first point to note is that because of the inconsistent relationship with neuromuscular disease patients may actually present with arrhythmias or conduction block [46,52]. Myotonic dystrophy is thus an important disorder to be considered in such patients and it is useful to bear in mind that their neuromuscular symptoms may be mild or unrecognised. In less typical cases such as these mutation analysis to look for the triplet repeat can be a useful adjunct to more traditional investigations.

The extent of the problem in myotonic dystrophy is uncertain, but from pathological findings and considering that the underlying defect is at a fundamental level it is quite possible that most, if not all, people with the classical form of myotonic dystrophy have some degree of cardiac pathology even if this is not of a degree to cause symptoms or ECG changes. Liaison with a cardiologist interested in the disorder would be useful.

Patients are usually asymptomatic, but should be specifically questioned as to the presence of fainting, blackouts, palpitations and breathlessness. Physical examination may reveal more—bradycardia, AF, frequent ectopics, mitral valve prolapse. A standard 12-lead ECG may reveal some of the features described above and, because of the progressive nature of the disease, should be done at least every 12 months. Because of the paroxysmal nature of arrhythmias and conduction abnormalities there should be a low threshold for using a 24 h Holter monitoring tape if either symptoms or ECG abnormalities are present and there may be a case for this being done in all patients. Few papers actually show the incidence of intermittent defects with the presence of 12-lead ECG abnormalities [35], although it would be useful to know the extent to which abnormalities are only found on 24 h tape and not on the 12-lead ECG. Signal-averaged electrocardiography [55] has been used to measure predisposition to cardiac arrhythmias [54,55]. These had previously been used to predict re-entry ventricular arrhythmias after myocardial infarction. In the latter study [53] myotonic dystrophy patients without bundle branch block were compared with 47 healthy subjects using late potentials: 34% of patients met two or more criteria for abnormal late potentials compared with 8% of controls. They were present in 6 of 8 cases with complex ventricular arrhythmias, including the only two with ventricular tachycardia, but were also present in 12 other cases. So, although sensitive to the presence of ventricular arrhythmias, they were not specific and so had a high false-positive predictive value.

Once a cardiac problem has been detected, the next question is how it should be managed. This is a difficult point and as yet there is no evidence to base answers on. However, the following points should be considered:

1. Because of their muscular impairment people with myotonic dystrophy do have a tendency to fall – which needs to be remembered when considering the use of warfarin in patients with AF. Again their disability also makes it more difficult for them to attend anticoagulant clinics.
2. Myotonic heart disease rarely causes significant chronic morbidity, but it is a significant cause of mortality with a substantial proportion of patients suffering sudden death, not all of whom are severely affected in other ways. Both complete heart block and ventricular tachyarrhythmias may be the causative factor. There are several reports of VT causing sudden death and it is likely that ventricular tachyarrhythmias account for more cases than was originally realised.
3. Cardiac disease in myotonic dystrophy is progressive.
4. Awareness of cardiac disease is especially important when considering procedures under anaesthetic. Myotonic dystrophy is well known for the respiratory and neuromuscular problems associated with anaesthesia, but previously latent arrhythmias or conduction block may also be revealed [46,57]. This can be both peri- and postoperatively, and may be precipitated by the extra stress of the operation or by the effects of a chest infection and subsequent hypoxia. The respiratory centre in myotonic dystrophy appears to be extremely sensitive to opiates and inducing agents and it is quite possible that these could also exert a central cardiovascular depressant effect [58]. In addition to investiga-

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tion of their cardiac status prior to operation such patients should receive cardiac monitoring during an operation and for at least 24 h afterwards, in an ITU or HDU environment, and it is important to emphasise that this is often the time when complications will occur. The usual precautions with regard to drugs used should be adhered to [5,56], and efforts to prevent (or at least prompt treatment of) chest infections, should be made.

These considerations would give a lower threshold than usual for permanent pacemaker insertion, and especially for use of a temporary pacemaker during an anaesthetic. When treating arrhythmias, it is useful to remember that interventricular conduction delay may also be present when deciding on which drugs to use. The most uncertain factor in management is when a predisposition to VT is shown as the risk/benefit value of prophylactic use of antiarrhythmic drugs or of an implantable defibrillator is uncertain. Similarly the arrhythmogenic effects of other drugs (e.g., tricyclic antidepressants) should be taken into consideration.

Congestive cardiac failure is rare and usually a late event in the natural history of myotonic heart disease. There is no suggestion that it needs to be treated differently than in any other patient.

Two areas where cardiac disease may also be important are in pregnancy and in congenital myotonic dystrophy.

5.1. Pregnancy and myotonic heart disease

There are few reports of myotonic heart disease in pregnancy. It might be expected that the extra stresses on the cardiovascular system caused by the increase in total blood volume during pregnancy would exacerbate any subclinical heart failure if this were present in myotonic dystrophy. The only report of heart failure in pregnancy is that of a 25-year-old woman in whom myotonic dystrophy was diagnosed at 5 weeks of gestation, after the diagnosis in her sister [45,59]. At 32 weeks she developed biventricular failure. Cardiac biopsy showed specific changes of myotonic dystrophy and excluded an inflammatory myocarditis. She initially responded to frusemide and digoxin but later needed continuous arteriovenous haemofiltration and delivery by Caesarean section. She was then treated with captopril and soon discharged. Eight weeks after delivery she died at home after a cardiac arrest. As this is the only case of peripartum heart failure in myotonic dystrophy, it is debatable whether it was secondary to myotonic dystrophy or whether, if myotonic dystrophy can be discounted as a cause of heart failure in pregnancy, it was idiopathic peripartum cardiomyopathy.

5.2. Congenital myotonic dystrophy and heart disease

There have been few studies of heart disease in congenital myotonic dystrophy. During childhood ECG abnormalities are rare with respiratory and neurological complications playing a larger role, but cardiac complications appear during adult life. In one study [60] 6 out of 7 patients with congenital myotonic dystrophy surviving into adulthood had conduction disturbances, but none had arrhythmia or QT prolongation. Another study [61] of the natural history of congenital myotonic dystrophy showed that 3 and 6 of 44 deaths were due to cardiac disease and sudden death, respectively. It also illustrated that monitoring of these patients from a cardiac point of view is unsatisfactory as only 10% of patients had had an ECG in the last year.

6. Future questions

There are unanswered questions concerning myotonic heart disease. The possibility that it is more common in certain families needs to be verified. Although several series have been done, the long follow-up time necessary to see changes means it is still very much guesswork as to how a known cardiac abnormality will progress in a patient.

Further studies on the correlation of the abnormal triplet repeat with cardiac disease would be useful especially if these included repeat size as measured from cardiac tissue; this presents obvious practical problems in numbers and selection of patients.

DMK appears to be associated with the intercalated discs, but the specificity of the antibodies used to investigate this needs to be confirmed. Further delineation of its role and the effect of the myotonic dystrophy mutation on it is uncertain, although a role in glucose utilisation would fit with the abnormalities seen.

Further, more detailed understanding of the way in which the gene functions, possible effects on nearby genes and the contribution of other genes to the cardiac phenotype will all be helpful.

The stage at which intervention in the form of pacemakers, implantable ventricular defibrillators, or prophylactic anti-arrhythmic drugs is very uncertain. This is partly because myotonic dystrophy is relatively rare, so there are not many units specialised in dealing with the cardiac problems of myotonic dystrophy and trials have not been done. Multicentre trials would be the only way of proceeding if evidence concerning various cardiological interventions is to be obtained.

Answers to these questions would help to target patients at particular risk of cardiac disease and may suggest possible interventions that would improve prognosis. Meanwhile cardiologists and others managing heart disease should be aware of the important cardiac problems that myotonic dystrophy patients may have, and that this is a not infrequent disorder that may present with cardiac rather than neurological symptoms.

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Acknowledgements

We would like to express our thanks to the Medical Research Council and the Muscular Dystrophy Group of Great Britain for their financial support, and to Dr. S. Davies, Institute of Medical Genetics, Cardiff, for her encouragement and advice in preparing this manuscript.

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