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Clinical Aspects of Arrhythmias

Definition of Arrhythmia

Arrhythmias are defined as **any cardiac rhythm other than the normal sinus rhythm.** Sinus rhythm originates in the sinus node. The electrocardiographic characteristics of normal sinus rhythm are:

- An impulse originated in sinus node initiates a positive P wave in I, II, VF, V_2-V_6, and positive or ± in leads III and V_1 that is transmitted through the atria, the atrioventricular (AV) junction, and the intraventricular specific conduction system (ISCS).
- In the absence of pre-excitation, the PR interval ranges from 0.12 to 0.20 s.
- At rest, the sinus node discharge cadence tends to be regular, although it presents generally slight variations, which are usually not evident by palpation or auscultation. However, under normal conditions, and particularly in children, it may present slight to moderate changes dependent on the phases of respiration, with the heart rate increasing with inspiration.
- In adults at rest, the rate of the normal sinus rhythm ranges from 60 to 80 beats per minute (bpm). Thus, sinus rhythms over 80 bpm (sinus tachycardia) and those under 60 bpm (sinus bradycardia) may be considered arrhythmias. However, it should be taken into account that sinus rhythm varies throughout a 24-h period, and sinus tachycardia and sinus bradycardia usually are a physiologic response to certain sympathetic (exercise, stress) or vagal (rest, sleep) stimuli. Under such circumstances, the presence of these heart rates is normal.
- As already stated, it is normal to observe a certain variation of the heart rate during 24 hours. Thus, the evidence of a completely fixed heart rate both during the day and at night is suggestive of arrhythmia. In addition, it is important to remember that:
  (i) **The term arrhythmia does not mean rhythm irregularity**, as regular arrhythmias can occur, often with absolute stability (flutter, paroxysmal tachycardia, etc.), sometimes presenting heart rates in the normal range, as is the case with the flutter 4×1. On the other hand, some irregular rhythms should not be considered arrhythmias (mild to moderate irregularity in the sinus discharge, particularly when linked to respiration, as already stated).
  (ii) **A diagnosis of arrhythmia in itself does not mean evident pathology**. In fact, in healthy subjects, the sporadic presence of certain arrhythmias, both active (premature complexes) and passive (escape complexes, certain degree of AV block, evident sinus arrhythmia, etc.) is frequently observed.

Classification

There are different ways to classify cardiac arrhythmias:

- **According to the site of origin**: arrhythmias are divided into supraventricular (including those having their origin in the sinus node, the atria, and the AV junction), and ventricular arrhythmias.
- **According to the underlying mechanism**: arrhythmias may be explained by (i) abnormal formation of impulses, which includes increased heart automaticity (extrasystolic or parasystolic mechanism) and triggered electrical activity, (ii) reentry of different types, and (iii) decreased automaticity and/or disturbances of conduction (see Chapter 3).
- **From the clinical point of view** arrhythmias may be **paroxysmal, incessant, or permanent**. In reference to tachyarrhythmias (an example of an active arrhythmia, see later), paroxysmal tachyarrhythmias occur suddenly and usually disappear spontaneously (i.e., AV junctional reentrant paroxysmal tachycardia); permanent tachyarrhythmias are always present (i.e., permanent atrial fibrillation); and incessant tachyarrhythmias are characterized by short and repetitive runs of supraventricular (Figure 4.21) or ventricular (Figure 5.4) tachycardia. Extrasystoles may also occur in a paroxysmal or incessant way (see Chapter 3, Mechanisms Responsible for Active Cardiac Arrhythmias). Some bradyarrhythmias,

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such as advanced AV block (an example of passive arrhythmia, see later), may also occur in a paroxysmal or permanent form.

- **From an electrocardiographic point of view**, arrhythmias may be divided into two different types: active and passive (Table 1.1):
  - **Active arrhythmias** due to increased automaticity, reentry, or triggered electrical activity (see Chapter 3 and Table 3.1) generate isolated or repetitive premature complexes on the electrocardiogram (ECG), which occur before the cadence of the regular sinus rhythm. The isolated premature complexes may be originated in a parasystolic or extrasystolic ectopic focus. The extrasystolic mechanism presents a fixed coupling interval, whereas the parasystolic presents a varied coupling interval. Premature complexes of supraventricular origin (p′) are generally followed by a narrow QRS complex, although they may be wide if are conducted with aberrancy. The ectopic P wave (P′) is often not easily seen as it may be hidden in the preceding T wave. In other cases the premature atrial impulse remains blocked in the AV junction, initiating a pause instead of a premature QRS complex (Figures 4.1C and 7.3). The premature complexes of ventricular origin are not preceded by an ectopic P wave, and the QRS complex is always wide (≥0.12 s), unless they originate in the upper part of the intraventricular specific conduction system (see Chapter 5, Electrocardiographic Diagnosis).

    Premature and repetitive complexes include all types of supraventricular or ventricular tachyarrhythmias (tachycardias, fibrillation, flutter). In active cardiac arrhythmias due to reentrant mechanisms, a unidirectional block exists in some part of the circuit (Figure 3.6).
  - **Passive arrhythmias** occur when cardiac stimuli formation and/or conduction are below the range of normality due to a depression of the automatism and/or a stimulus conduction block in the atria, the AV junction, or the specific intraventricular conduction systems (ICS).

    From an electrocardiographic point of view, many passive cardiac arrhythmias present isolated late complexes (**escape complexes**) and, if repetitive, slower than expected heart rate (bradyarrhythmia). Even in the absence of bradyarrhythmia, some type of conduction delay or block in some portion of the specific conduction system (SCS) may exist, for example, first-degree or some second-degree sinoatrial or AV blocks, or atrial or ventricular (bundle branch) blocks. The latter encompasses the aberrant conduction phenomenon (see Chapter 3, Aberrant Conduction). Thus, the electrocardiographic diagnosis of passive cardiac arrhythmia can be made because it may be demonstrated that the ECG changes are due to a depression of automatism and/or conduction in some part of the SCS, without this manifesting in the ECG as a premature complex, as it does in reentry (Figure 3.6).
- Atrial or ventricular blocks are not usually considered arrhythmias. But in our opinion, they should be included as passive cardiac arrhythmias like other types of blocks (sinoatrial or AV). This is why they have been included in this book (see Chapter 3, Heart Block, and Chapter 6, Atrial Blocks, and Ventricular Blocks).

Table 1.1 Classification of arrhythmias according to their electrocardiographic presentation.

Active arrhythmias	Passive arrhythmias
Supraventricular	Escape complex
• Premature complexes	Escape rhythm
• Tachyarrhytmias	Sinus bradycardia
– Different types of tachycardia	Sinoatrial block
– Atrial fibrillation	Atrial block
– Atrial flutter	Atrioventricular block
• Ventricular	Ventricular block
• Premature complexes	Aberrant conduction
• Different types of tachycardia	Cardiac arrest
• Ventricular flutter	
• Ventricular fibrillation	

Clinical Significance and Symptoms

The incidence of the majority of arrhythmias increases progressively with age and arrhythmias are not frequent in children. Data from the Holter ECG recordings (see Appendix A-3, Holter electrocardiographic monitoring and related techniques) have demonstrated that isolated premature ventricular complexes (PVC) are present in about 10–20% of young people in 24-h recordings, and their presence is nearly a rule in the 80+ age group. Similarly, sustained chronic arrhythmias, such as atrial fibrillation, are exceptional in children and are present in about 10% of subjects over 80 years of age. However, **there are arrhythmias that arise particularly in children**, such as some paroxysmal and incessant AV junctional reentrant tachycardias (AVJRT), as well as some monomorphic ventricular tachycardias (idiopathic) and polymorphic ventricular tachycardias (catecholaminergic).

In this book devoted to providing the basis for the diagnosis, prognosis, and treatment of arrhythmias, **active and passive classification of arrhythmias** is used (Table 1.1):

- Active cardiac arrhythmias include isolated or repetitive impulses that command heart rhythm, instead of the basic normal sinus rhythm. They are recorded on the ECG tracing as isolated (premature supraventricular or ventricular complexes), repetitive (named runs), or sustained complexes (different types of tachyarrhythmias).
- Many passive cardiac arrhythmias show isolated or repetitive sinus or escape complexes in the ECG tracings with an abnormally slowed heart rate (bradyarrhythmias). This may be due to depression of automaticity or sinoatrial or AV block. However, in some cases the mechanism responsible for the passive cardiac arrhythmia is delayed conduction, which may modify the ECG pattern (first-degree AV block, or atrial or ventricular bundle branch block), but this does not mean that the heart rate has to be slow.

The most important clinical significance of arrhythmias is related to an association with sudden cardiac death (Goldstein *et al*., 1994; Recommended General Bibliography p. xvii). It is also important to remember that frequently arrhythmias (especially atrial fibrillation) may lead to embolism, including cerebral emboli, often with severe consequences. Also, it must be remembered that sometimes fast arrhythmias may trigger or worsen heart failure (HF). These aspects will be commented on.

Arrhythmias and Sudden Death (SD)

Some of the most important aspects of SD, a true epidemic of the twenty-first century, will now be examined here. In other parts of the book (Chapters 8–11) specific aspects of SD in relation to different heart diseases or situations are discussed in more detail.

Epidemiology

Sudden death is probably the most challenging issue in modern cardiology, taking into account the remarkably high number of SD cases (the estimated number of SD in the United States is approximately 400 000 cases per year, although in Mediterranean countries, such as Spain, the incidence is lower) (Keys and Keys, 1975; Masiá *et al*., 1998; Marrugat *et al*., 1999; Sans *et al*., 2005) and the important social impact of SD events.

Even though SD has been reported in newborns, in whom it has been related to repolarization disorders, alterations of the autonomic nervous system (ANS), and an increase of vagal tone (see Chapter 11, Sudden Infant Death Syndrome), it is indeed very rare in the first decades of life. At this age it often occurs during sports activities (Bayés de Luna *et al*., 2000) and is often associated with inherited heart disease (hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia/cardiomyopathy, and channelopathies). The incidence of SD gradually but significantly increases after 35–40 years of age and is particularly high during the acute phase of myocardial infarction (MI). It is also frequent during the chronic phase of ischemic heart disease (IHD), as well as in subjects with any heart disease, especially when heart failure (HF) is present (Myerburg *et al*., 1997) (Figure 1.1).

Associated Diseases

As previously discussed, acute IHD is frequently associated with SD in adults. In the majority of cases of SD outside acute IHD or channelopathies, HF, or at least left ventricular dysfunction, is present. HF may be idiopathic or present in patients with chronic IHD, hypertension, cardiomyopathies, and so on. More details on this association are shown in Chapter 11 (see Chapter 11, Ischemic

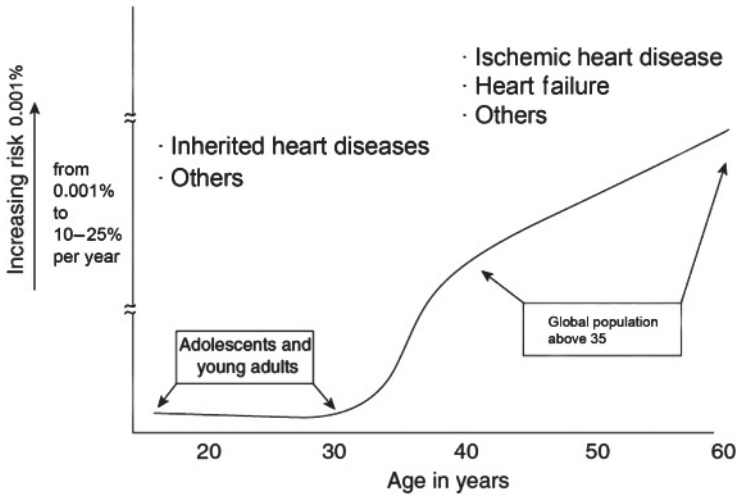

Figure 1.1 Relationship between the incidence of sudden death (SD) and age. Note that the sudden death may also be associated with different diseases along the life period (Myerburg *et al*., 1992).

Heart Disease, and Heart Failure). Inherited heart disease (InHD) can cause SD at any age but the overall impact is small (Figure 1.1). It should be emphasized, however, that it is responsible for the majority of cases of SD that occur before the age of 35 years. InHD appears more in men and may occur during exercise (cardiomyopathies) or sleep or rest (channelopathies) (see Chapter 9).

We performed a study (the EULALIA trial) that included 204 cases of SD occurring in the Mediterranean area (Subirana *et al*., 2011). In this study, the epidemiological and pathological aspects of diseases associated with SD were analyzed. Table 1.2 shows the diagnosis obtained by the pathologists. When compared with other similar Anglo-Saxon studies (Burke *et al*., 1997), what caught our attention was that the number of cases presenting with IHD found at autopsy, as well as the incidence of acute thrombosis, as an anatomopathologic expression of MI, was lower than in previously published Anglo-Saxon studies (80–90% vs 58% and 52% vs 40% for IHD and acute thrombosis, respectively) (Figure 1.2). Our findings are concordant with previously known evidence (Keys and Keys 1975; de Lorgeril *et al*., 1999; Marrugat *et al*., 1999; Sans *et al*., 2005) that the incidence of IHD in Mediterranean regions is lower, probably related to diet, lifestyle, and environment (Mediterranean culture). In contrast, SD victims from the Mediterranean region presented left ventricular hypertrophy more frequently than other studies (48% vs 20%) (Virmani *et al*., 2001; Subirana *et al*., 2011). From a clinical point of view, the victims of SD in the EULALIA trial presented anginal episodes less frequently (20% vs 37%), which was in agreement with the reduced number of cases with IHD found at autopsy, when compared with the Maastricht study (de Vreede-Swagemakers *et al*., 1997). In our series, the incidence of associated InHD was 3% (hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy). In approximately 7% of cases autopsy did not reveal any changes. Some of these cases might be explained by channelopathies (Table 1.2).

Table 1.2 Sudden death victims: pathological abnormalities found in necropsy.

Sudden death victims (n = 204)	N	%
Cardiovascular diseases (n = 183)		
Heart diseases (n = 161)		
Ischemic heart disease	119	58.4
Hypertensive heart disease	20	9.9
Valvular diseases	5	2.4
Idiopathic left ventricular hypertrophy	4	1.9
Dilated cardiomyopathy	4	1.9
Hypertrophic cardiomyopathy	3	1.5
Arrhythmogenic RV dysplasia/ cardiomyopathy	3	1.5
Myocarditis	1	0.5
Congenital heart disease	1	0.5
Amyloidosis	1	0.5
Vascular diseases (n = 22)		
Pulmonary embolism	8	3.9
Dissection of the aorta	9	4.4
Cerebral hemorrhage	5	2.4
Nonvascular diseases (n = 7)		
Gastrointestinal disorders	3	1.5
Pulmonary disorders	4	1.9
Without findings	14	6.9

Taken from Subirana *et al*., 2011.

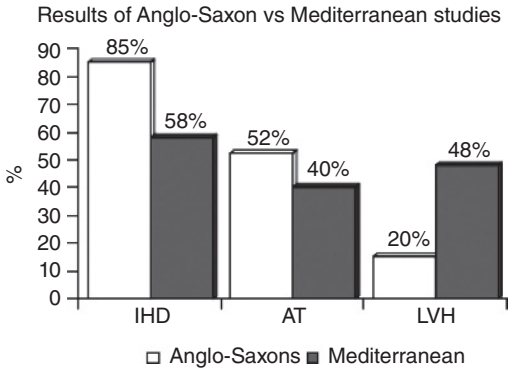

Figure 1.2 Comparative study on the incidence of ischemic heart disease (IHD), acute thrombosis (AT), and left ventricular hypertrophy (LVH) in the EULALIA trial.

The majority of SD cases occur in subjects with ischemic heart disease and/or heart failure. It must be emphasized that heart failure is most frequently related to hypertension, chronic ischemic heart disease, cardiomyopathies, and valvular heart disease.

Inherited heart diseases are the main cause of SD in the first decades of life.

Chain of Events Leading to Final Arrhythmias and SD

SD is the final stage of a chain of events that ends in cardiac arrest, usually due to ventricular fibrillation (VF) or, less frequently, extreme bradyarrhythmia (Bayés-Genis *et al*., 1995). In all cases there are a number of modulating and/or triggering factors that act on the vulnerable myocardium precipitating SD. Figure 1.3 shows this chain of events in different heart diseases. Ventricular fibrillation (VF) can appear without previous VT, triggered by a PVC in the presence of other modulating or triggering factors (including genetic and environmental),

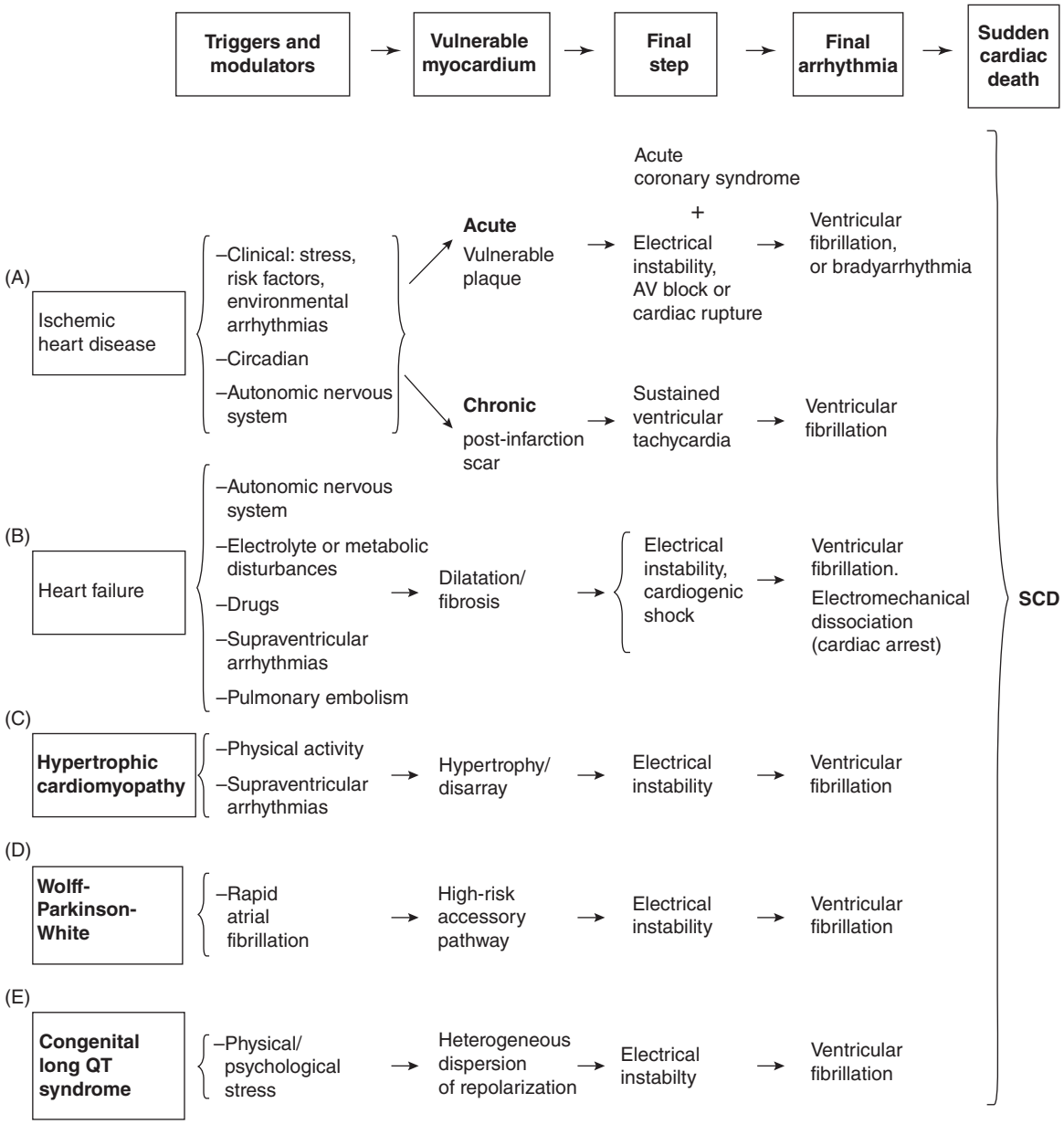

Figure 1.3 Chain of events that trigger cardiac sudden death (CSD) and parameters that different diseases present at the different stages leading to CSD (adapted from Bayés-Genis *et al*., 1995).

and/or the sympathetic overdrive secondary to physical or mental stress. Usually under normal circumstances, probably all of these factors would not be of any consequence, but in the presence of acute ischemia they may trigger SD (Figure 1.5). The VF may be secondary to classic monomorphic sustained VT (Figure 1.4) or Torsades de Pointes VT (Figure 1.6). Sudden death is seldom a consequence of bradyarrhythmia (Figure 1.7).

Therefore, the final arrhythmias that precipitate SD are not always the same (Figures 1.4–1.8). In a study that we performed revising the final causes of SD in 157 ambulatory patients who died suddenly while wearing a Holter recorder (Bayés de Luna *et al*., 1989), it was found that in two-thirds of patients SD was caused by **sustained VT that precipitated** VF (Figure 1.8, Table 1.3). This was generally accompanied by fast baseline heart rate (sinus tachycardia or rapid atrial fibrillation), which may be considered a sign of sympathetic overdrive (Figure 1.4). VF without previous VT, usually associated with acute IHD, is more frequently seen as a consequence of PVCs with an R/T phenomenon. In our experience with ambulatory patients this pattern was observed in less than 10% of cases (Figure 1.5). Curiously, in 13% of cases, SD was due to Torsades de Pointes VT precipitating VF, generally

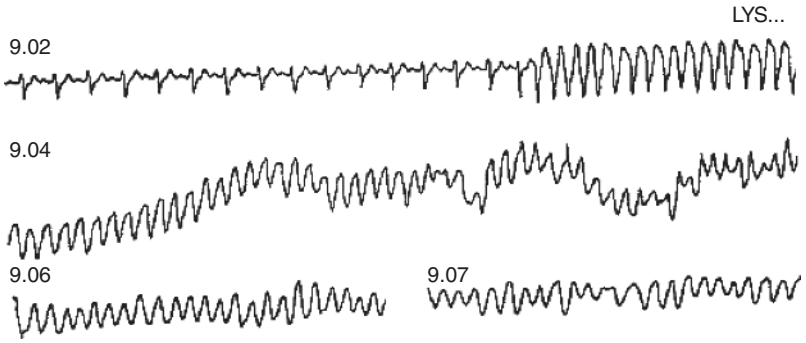

Figure 1.4 Ambulatory sudden death due to a ventricular fibrillation (VF) in an ischemic heart disease patient treated with amiodarone for frequent premature ventricular complexes. At 9:02 a.m. he presented a monomorphic sustained ventricular tachycardia (VT), followed by a VF at 9:04 a.m. after an increase in VT rate and width of QRS complex.

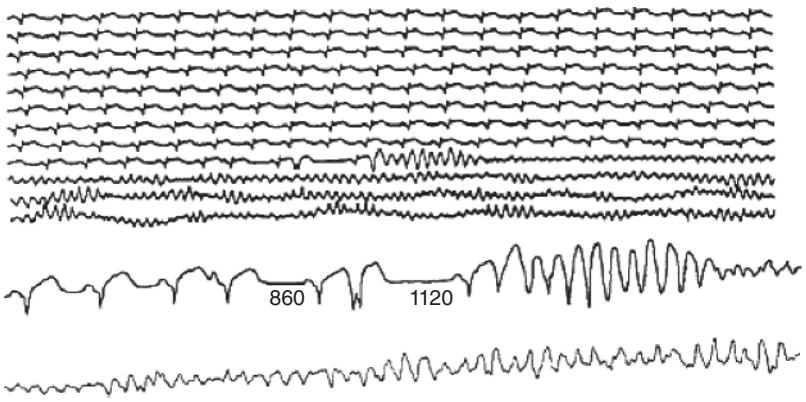

Figure 1.5 Ambulatory sudden death due to a primary ventricular fibrillation (VF) triggered by a premature ventricular complex (PVC) with a short coupling interval, after a post-PVC pause (1120 ms) longer than the previous one (860 ms). Note that the sequence of events started with an atrial premature complex, which caused the first shorter pause.

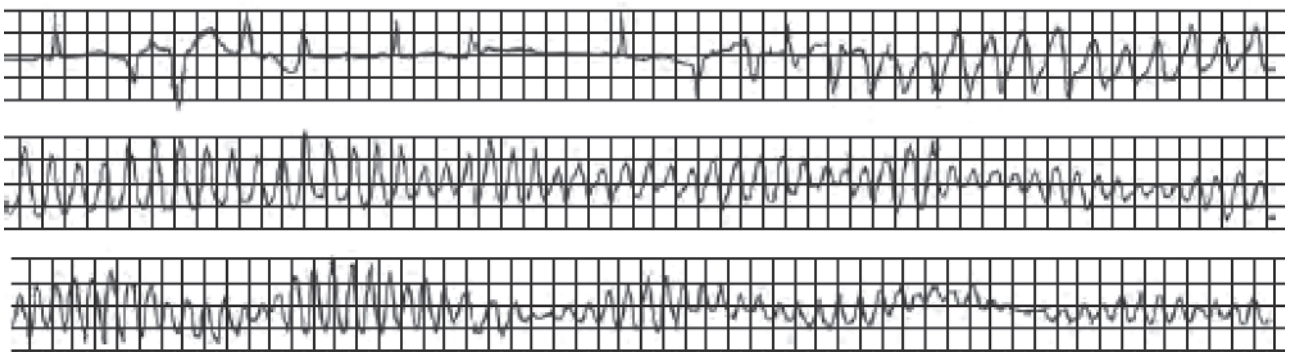

Figure 1.6 Beginning of a Torsades de Pointes ventricular tachycardia (VT) in a woman without ischemic heart disease treated with quinidine for runs of nonsustained VT. The Torsades de Pointes VT triggered a ventricular fibrillation (VF).

in patients without severe heart disease but taking antiarrhythmic Class I type drugs because of nonfrequent ventricular arrhythmias, sometimes isolated PVCs (proarrhythmic effect). We believe that if this study were performed now, the number of cases would be much smaller due to the evidence shown by the CAST study (Echt *et al*., 1991) demonstrating that class I antiarrhythmic agents are dangerous, especially in patients with heart disease. Thus, currently the prescription of class I antiarrhythmic drugs in post-MI patients is much lower. Finally, cases of SD due to extreme bradyarrhythmia (≈15% in our study) (Figure 1.8B) were related more to progressive depression of the sinus node and AV node automatism (Figure 1.7) than to AV block.

Figure 1.8 shows the final arrhythmias that cause SD in patients with different clinical settings: (A) in a mobile coronary care unit on route to hospital due to an acute coronary syndrome (Adgey *et al*., 1982), (B) in ambulatory patients (Holter recording) (Bayés de Luna *et al*., 1989), and (C) in patients hospitalized because of severe HF (Luu *et al*., 1989). In the first situation (A), there are more cases of without previous VT than in our ambulatory cohort (B), most probably because patients in group A were in the acute phase of a MI. On the other hand,

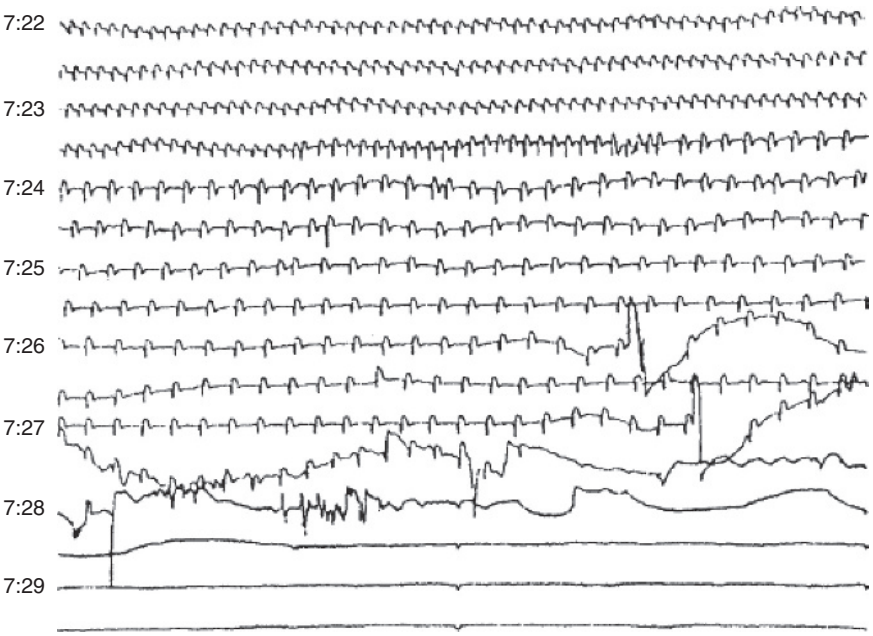

Figure 1.7 Sudden death due to a progressive bradycardia in a patient with acute infarction and electromechanical dissociation.

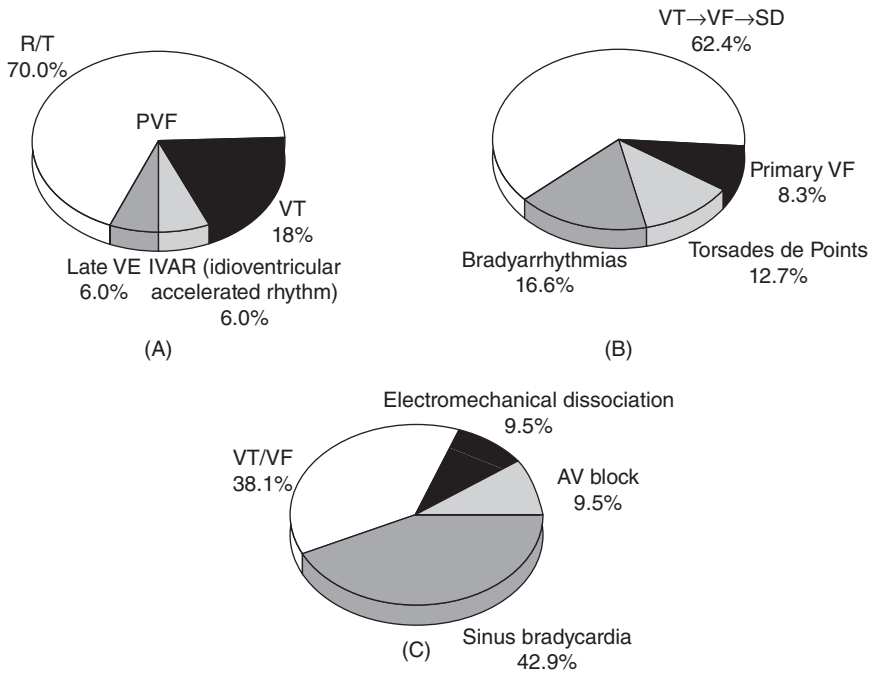

Figure 1.8 Sudden death: final arrhythmias. (A): in patients with acute ischemic heart disease (Adgey *et al*., 1982). (B): in ambulatory patients wearing a Holter monitor, in whom a depressed ejection fraction was present in 80% of cases (Bayés de Luna *et al*., 1989). (C): in patients with advanced heart failure (Luu *et al*., 1989).

patients with severe HF (group C) presented extreme bradyarrhythmias more frequently as a cause of SD. This could be the reason why antiarrhythmic drugs are not efficient in preventing SD in patients with severe HF. In our series (Figure 1.8B), 80% of patients had a depressed ejection fraction (EF), although their functional class was acceptable. These patients were "too healthy to die", and many of these cases of SD could have been prevented with adequate therapy that sometimes consists of not prescribing an antiarrhythmic agent. The Hippocratic Oath must be remembered: "c", "First, do no harm".

Our results were similar to those demonstrated in patients treated with implantable cardioverter defibrillators (ICD) with or without cardiac resynchronization therapy (CRT) (ICD-CR). In these cases, fast VTs also frequently appeared and were treated by antitachycardia pacing (Leitch *et al*., 1991; Grimm *et al*., 2006). In contrast, in a small series of post-MI patients with an EF <40%, using an insertable loop recorder, who died

Table 1.3 Clinical characteristics of patients who died suddenly while wearing a Holter device.

	Ventricular tachyarrhythmias		
	Group I Primary VF and	**Group II Torsades de**	**Group III**
	VT → VF n = 143	**Pointes n = 43**	**Bradyarrhythmias n = 48**
Age (years)	70	60	70
Gender (males) (%)	76	40	39
IHD patients (%)	84	50	70
With no known heart disease (%)	4	22	10
Resuscitated (%)	20	28.5	4
Antiarrhythmic therapy (%)	64	76	–

IHD, ischemic heart disease; VF, ventricular fibrillation; VT, ventricular tachycardia. Taken from Bayés de Luna *et al.*, 1989.

suddenly it was demonstrated that vast majority of SD were primary VF not triggered by VT. However, information about clinical events surrounding the time of death was not known. This lack of information and the small number of cases make it difficult to compare this series with our results. In the majority of patients who died due to different types of bradyarrhythmia, death occurred more than one hour after the onset of symptoms (Gang *et al.*, 2010).

How to Identify Patients at Risk

We know much more about identifying subjects at risk for SD within the group of high-risk patients (history of cardiac arrest, inherited cardiomyopathies, some post-infarction patients, heart failure, etc.) than in the general population in which SD often represents the first manifestation of the disease (Moss *et al.*, 1979; Théroux *et al.*, 1979; Myerburg *et al.*, 1992, 1997). Figure 1.9 shows that these cases (A and B) represent more than 50% of all SD events. Many of these cases represent patients with first acute MI.

As it is impossible to carefully screen the entire general population, it is very difficult to identify subjects with no previous cardiovascular symptoms and no apparent risk factors who are at risk for SD. Currently, what should be done is to perform the following tasks: (i) a detailed study of relatives of SD patients; (ii) when seeing a patient for whatever reason, ask whether there are any family members who have had IHD, InHD, or present evident risk factors; and (iii) perform a complete physical examination and blood test (testing for risk factors, especially cholesterol and blood glucose) and take a blood pressure and an ECG recording when an adult is visited for the first time.

Trying to identify the subjects at risk for SD is one of the biggest challenges of modern cardiology. In the Framingham study performed on a general population (Kannel and McGee, 1985), two things were demonstrated: (i) the

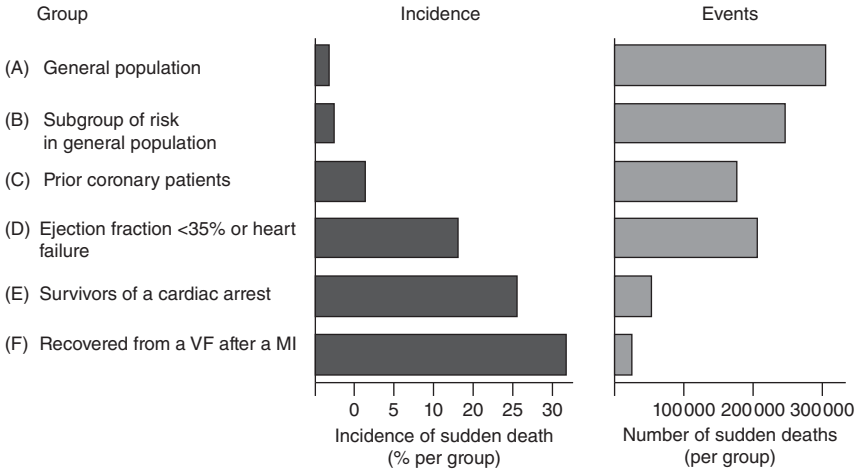

Figure 1.9 Left: the percentage of patients with SD is much higher in the high-risk groups (D–F) than in the general population (A, B). The total amount of cases occurring in the general population is greater than the number of all other subgroups of patients at risk (Myerburg *et al.*, 1997).

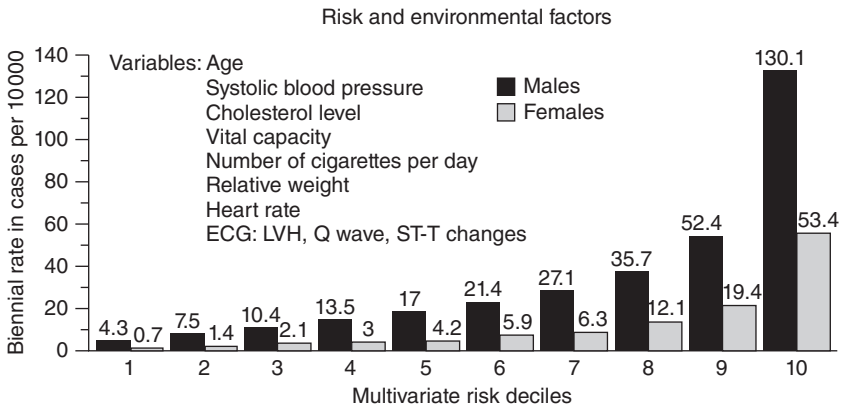

Figure 1.10 Risk of sudden death (SD) in the Framingham study according to multivariate risk (see inner note) in males and females (Kannel and McGee, 1985).

presence of alterations in the ECG, especially the bundle branch block, and left ventricular hypertrophy significantly increases the risk of SD, mainly in men; and (ii) in a multivariate analysis, the risk of SD increased especially in men, in relation to the amount of risk factors they had (Figure 1.10). Recently, it has been demonstrated that an increase of N-terminal prohormone brain natriuretic peptide (NT-proBNP) levels suggest, more than other previously described biochemical risk factors (dyslipidemia), an increased risk of sudden death in women (Korngold *et al*., 2009) and in patients with heart failure (Vazquez *et al*., 2009).

Risk stratification by an estimated calcium "score" by multislice computed tomography (CT) scan may help to identify patients with asymptomatic IHD. Nevertheless, this method is not currently recommended as a routine test (Greenland *et al*., 2000), although it might be useful in patients with multiple risk factors (ATP III Guidelines 2001). The latest ACC and Associated Societies statement does not support the application of this technique in the general population and raises doubts as to whether this test should even be performed in medium- and high-risk patients (Hendel *et al*., 2006). Also, its indiscriminate use is not recommended by other authors (Bonow 2009). In our opinion, in middle-aged patients with significant family history and/or multiple risk factors, it may be useful to perform the calcium "score" and, if positive, use a noninvasive coronarography by means of the latest generation multislice CT scan, which currently emits less radiation. Magnetic resonance imaging (MRI) offers more information on heart anatomy and function in a single test, and in a safer manner.

The difficulties in identifying subjects at risk for cardiac arrest are increased by the fact that the general population is more willing to perform medical examination to detect certain malignancies (colon, breast in women, and prostate in men). Adequate examinations, such as a multislice CT (in patients with a positive family history, and/or positive exercise test without symptoms or other risk factors) or genetic tests in special situations (young patients with a family history of SD, suspicion of channelopathies, etc.), to determine apparently silent patients at risk for SD have to be performed more frequently.

The third part of this book deals with different aspects related to SD in different heart diseases and situations. The mechanisms that trigger fatal arrhythmias and the characteristics of an anatomic or electrophysiologic substrate, if known, that make the myocardium vulnerable to VF/SD will be explained.

How to Prevent SD

Obviously, the best way to prevent SD is to identify subjects at risk (see above). In the group with the highest risk (Figure 1.9D–F) it may be necessary, even compulsory, to implant an ICD, (see Chapters 5, 8, and 9, and Appendix A-4). This alone does not prevent SD but may help to avoid it when the final arrhythmia appears.

Thus, it is known how to prevent sudden death in patients at high risk (Myerburg *et al*., 1992). It is much more difficult, however, to prevent SD events in the general population. The true prevention of SD is fighting the associated diseases, such as IHD, HF, and InHD Prevention of IHD should start in childhood, with an adequate health education promoting a healthy lifestyle, including controlled exercise, and an adequate diet to avoid overweight and obesity, preventing the development of risk factors. Of course, it is crucial to fight and treat high cholesterol, hypertension, diabetes, and other risk factors when they are present because they are, at least in part, responsible for the presence of atherosclerotic plaques. Also it is important, if possible, to avoid and treat HF adequately from the moment it starts, and it is necessary to diagnose and manage InHD This includes detailed personal and family history (history of syncope/SD), as well as the knowledge that a simple ECG pattern can identify a patient at risk for SD (see Chapter 9). When looking to the future, what is needed

to reduce the burden of SD is an arteriosclerotic plaque stabilizer, preferably a chemical additive to food or water, that may be given to the global population, to stabilize the fibrous cap of the plaque and reduce the probability of plaque erosion/rupture and SD (Moss and Goldenberg, 2010).

The Management of a Patient Resuscitated (Survivors) from a Cardiac Arrest

Patients resuscitated from an out-of-hospital cardiac arrest should be referred to a reference center for a detailed evaluation, in order to identify the cause of the cardiac arrest, using an exhaustive examination that includes noninvasive and, if necessary, invasive tests. This is the routine approach for patients who suffered a cardiac arrest with and without evident heart disease. A report (Krahn *et al*., 2009) recommends genetic testing only when a genetic disease appears to be responsible for cardiac arrest in the clinical test results. In our opinion, genetic studies need to be more accessible and cheaper. This would encourage their use and would be of great benefit regardless of their current limitations, in addition to studying the relatives of patients with InHD (see Chapter 9).

Ventricular fibrillation is the cause of cardiac arrest in most of the cases (Figure 1.8). Therefore, it is necessary to prevent the first episode and, in any case, to organize a proper plan to prevent future episodes. If VF appears to be associated with ischemia, the possibility of revascularization has to be considered (see Chapter 11, Chronic Ischemic Heart Disease). Other possible mechanisms involved in the triggering of VF have to be ruled out, that is, in rapid AF in patients with Wolff–Parkinson–White syndrome (WPW) in whom ablation of the accessory pathway is mandatory.

In many other cases of cardiac arrest due to VT/VF, if no trigger is found, it is usually necessary to implant an ICD with a resynchronization pacemaker (CRT), only if needed (see Chapters 9–11).

Obviously, in cardiac arrest due to passive arrhythmias, an urgent pacemaker implantation is required (see Chapter 6).

For more details about ICD indications/implantation see Chapters 5 (Ventricular Tachycardias, and Ventricular Fibrillation), 9, and 11 (Ischemic Heart Disease and Heart Failure), as well as Appendix A-4 (Automatic Implantable Cardioverter Defibrillator (ICD)), and guidelines of scientific societies (Recommended General Bibliography p. xvii).

Arrhythmias and Severe Clinical Complications

The relationship of active/passive arrhythmias with SD has been mentioned. Now, the other important clinical complications of tachy/bradyarrhythmias not associated to SD will be exposed. Tachyarrhythmias may induce severe consequences on the patient's clinical and hemodynamic status, which may appear as:

- A crisis of left ventricular failure, and also a congestive HF (tachycardiomyopathy).
- A crisis of angina (hemodynamic angina).
- A low cardiac output with dyspnea and weakness.
- Hypotension that may be significant, even resulting in cardiogenic shock.
- Embolism, more often systemic, frequently cerebral, sometimes with severe consequences. It has been recently demonstrated that not only a complete stroke but also cognitive impairment may be caused by cerebral microembolism in patients with sluggish left atrium related to AF or may be even in its absence but with stagment LA due to advanced IAB (Bayés de Luna *et al*., 2017).
- Dizziness, pre-syncope, syncope. Syncope may be benign or may be a marker of life-threatening arrhythmia (see later).

The most frequent symptoms related to bradyarrhythmia are a low cardiac output, dizziness, syncope, and even SD.

All the symptoms related to brady or tachyarrhythmias are especially important in relation to:

- The presence or absence of heart disease. An association with either acute ischemia or HF is of utmost importance.
- Duration of the arrhythmia; the longer it is, the greater the risk of not being well tolerated.
- Heart rate (fast tachycardia or severe bradycardia) during the arrhythmia. Consequently, an episode of short duration, with a not very fast heart rate in subjects without heart disease, does not affect the cardiac output, and it will not result in significant hemodynamic impairment. On the other hand, very rapid episodes, especially in patients with heart disease and poor ventricular function, may cause evident hemodynamic impairment resulting in dyspnea, hypotension (Figure 1.11), angina, syncope, and even shock and congestive HF if the arrhythmia is sustained.
- The presence or absence of AF dissotiation.

Some aspects of syncope, the most alarming symptom associated with arrhythmias, which may be of practical interest to the reader, will now be examined.

Syncope: Serious or Innocent Symptom?

Concept

Syncope is the sudden and transient loss of consciousness caused by an important reduction in cerebral

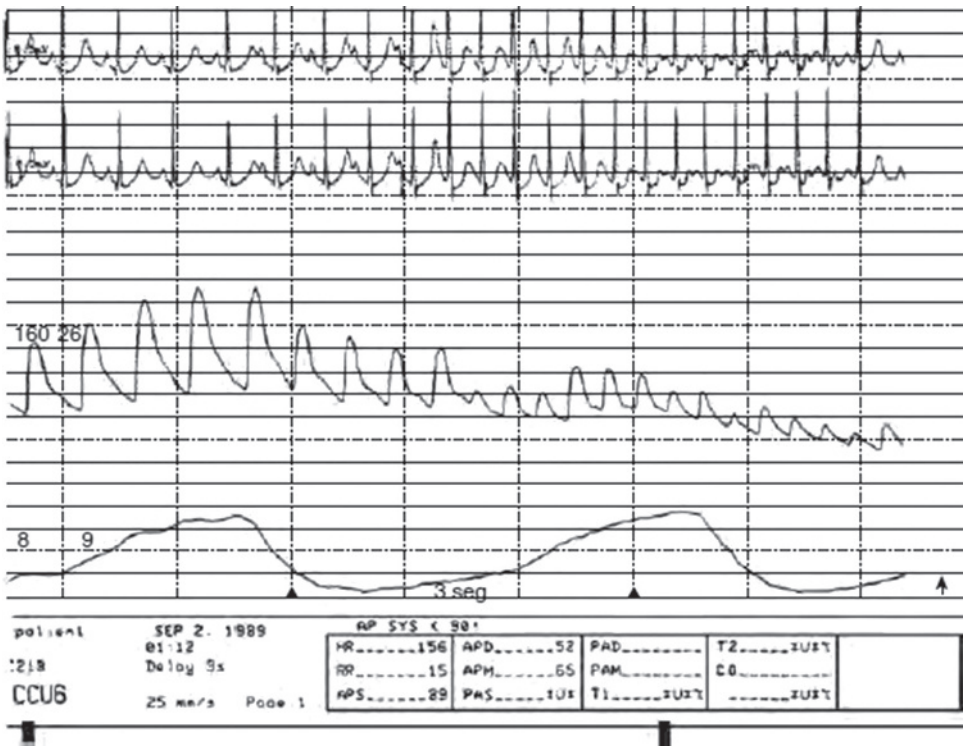

Figure 1.11 Note the drop of blood pressure coinciding with an abrupt rise of heart rate during a paroxysmal tachycardia.

perfusion. It is accompanied by loss of muscular tone and a total spontaneous recovery in a short period of time. At times there is only a feeling of dizziness or unsteadiness (pre-syncope) (Garcia Civera *et al*., 1989).

This is the most worrying symptom of patients with arrhythmias. It can be either the expression of an innocent process or a marker of evident risk of SD. From clinical and prognostic points of view, there are three types of syncope: (i) neuromediated via vagal reflex and those due to orthostatic hypotension that are usually benign; (ii) related to heart diseases, such as severe tachy- or bradyarrhythmia, or those due to obstruction of flow (aortic stenosis, or mixoma for example) (see later), which are usually malignant; and (iii) very short crisis of cerebral ischemia or epilepsies. In fact, clear transient ischemic attack (TIA) has to be excluded as one type of syncope (see later). These different types of syncope are examined, as are the ways to cope with them. It must be remembered that syncope represents 1% of all cases attended to in an emergency department.

Mechanisms

- **Neuromediated reflex syncope**. A high percentage of syncopal episodes (>50%) are neuromediated via a vasovagal reflex, often with triggering factors related to increased vagal tone, such as cough, micturition, venous puncture, orthostatism, and so on. Recent studies have shown that some polymorphism of protein G is associated with family history and may explain the susceptibility to vasovagal syncope (Márquez *et al*., 2007; Lelonek *et al*., 2009). **Hypotensive orthostatic syncope** is frequent (10–20%). It is caused by a dysautonomy reflex during orthostatism, which produces a loss of vaso-constrictive reflexes in the vessels of the lower extremities, reducing baroreceptor sensitivity and producing reactive hypotension to such a degree that it decreases cerebral flow and induces syncope. **Hypersensitivity of the carotid sinus** (a pause >3 s, or a decrease in blood pressure >30 mm, that occurs after carotid sinus massage for 10 s with or without syncope) may also induce a neuromediated syncope via a vagal stimulus from a sick carotid sinus, and may be the cause of an unexplained fall, especially in the elderly. This syncope is often related to some accidental pressure on the carotid sinus (while shaving, for instance). Patients referred to a tilt test should have a carotid sinus massage performed. The association between neuromediated syncope and carotid sinus hypersensitivity is approximately 30%.
- **Syncopes of cardiac origin** include all syncopes related to arrhythmias (5–10%); they encompass bradyarrhythmias (sick sinus syndrome and advanced

AV block) and tachyarrhythmias (very fast supraventricular arrhythmias, i.e., pre-excited atrial fibrillation with WPW, sustained VT, and polymorphic VT of all types). These arrhythmias, which may trigger syncope and VF/SD, are seen especially in IHD, HF, and InHD (cardiomyopathies and channelopathies), as well as in other heart diseases and clinical situations (see Chapters 8–11). Also, syncopes of cardiac origin may be related to obstruction of flow obstruction (2–3%), as in aortic stenosis, hypertrophic cardiomyopathy (CM), mixoma, and so on.

- **Syncopes related to neurological disorders** in the past included the neurological disorders that may induce a brusque reduction in cerebral perfusion, which may happen in some transient ischemic attacks with loss of consciousness (subclavian steal syndrome or bilateral severe carotid artery stenosis). Usually they are accompanied by transient neurological problems (transient ischemic attack, etc.) but really they may not be considered a true syncope.

Diagnosis and Management of Patients with Syncope

Firstly, we have to be certain that the patient has experienced a syncopal episode. This means that all aspects of the definition of syncope must be present: abrupt and transient loss of consciousness, caused by a brusque reduction in cerebral flow, accompanied by a loss of muscular tone, followed by a total spontaneous recovery. The group of Bob Sheldon, in Canada, has published a series of articles in how to differentiate neuromediated syncope from seizures, and from other arrhythmic forms of syncope. The Calgary score helps physicians to discriminate benign from malignant forms of syncope using only interrogation tools (Sheldon *et al*., 2002, 2006, 2010).

Next, we must always rule out factors that may provoke prolonged unconsciousness, such as hysterical attacks, hypoglycemia, intoxication including alcohol (heavy drinkers), or dizziness and vertigo among others. We must also exclude epileptic episodes that sometimes produce problems of differential diagnosis, although history taking is very useful in general (see above). During epileptic attacks there is no reduction in cerebral perfusion; however, some infrequent epileptic forms may present arrhythmias with syncopal episodes and even SD following an epileptic convulsion (Rugg-Gunn *et al*., 2004; Tomson *et al*., 2008).

Syncopes may be accompanied by seizures (pallor, no pulse, rapid recovery with facial flush – Stokes–Adams crisis) and may occur at rest or, typically, during exercise (see Chapter 9). It must be emphasized that it is extremely important to differentiate neuromediated vasovagal syncopes, including orthostatic syncope, which are generally benign, from syncope due to cardiac origin that often present an unfavorable prognosis. The latter includes (see before) syncope due to very slow or very rapid arrhythmias, or an obstruction to flow (aortic stenosis, hypertrophic cardiomyopathy, myxoma, etc.).

To recognize the origin of syncope we will proceed to the basal study that includes history taking, physical examination, and an ECG (Figure 1.12). Depending on the results it may be necessary to perform other complementary tests.

Figure 1.12 shows the basal study that may be useful to diagnose and further manage a patient with syncopal attacks. Although history taking is very important, the information obtained through physical examination, the ECG, and other complementary tests is also often needed. However, sometimes history taking is practically definitive (especially in vasovagal neuromediated syncopes). For more information see the guidelines of scientific societies (Moya *et al*., 2009; McCarthy *et al*., 2009; Recommended General Bibliography p. xvii).

Not only is the electrocardiographic diagnosis of arrhythmias important, but so too is the medical context in which they occur. A paradigmatic example of this assertion is the fact that premature ventricular contractions having similar clinical and electrocardiographic characteristics are usually benign in healthy patients, whereas in patients with ischemic heart disease and poor ventricular function they represent an evident risk of sudden death, especially in the presence of acute ischemia.

Units of cardiac syncope have to be prepared to perform a tilt test. Indications for a tilt test have been limited to cases of syncope where the cause is not clear through extensive interrogation of triggers, clinical scenarios, and physical examination. It is still useful as an integral part of the study of the autonomic nervous system. A tilt test should not replace clinical judgement:

- It is important **to obtain a comprehensive history** (Colman *et al*., 2009), including: (i) family antecedents of syncope or SD, which is very important in attempting to rule out InHD; (ii) antecedents of previous heart disease (MI, history of valve heart disease, etc.); (iii) the number of prior syncopes, and in adults whether they also occurred during childhood; and (iv) the evaluation of: (a) the prodromal symptoms or circumstance of appearance (exercise, movements, digestion, emotions, etc.); (b) the onset (abrupt or slightly gradual); (c) the position in which they occur, such as standing (orthostatic hypotension) or sitting; (d) what the patient was doing before (cough, defecation, micturition, carotid sinus massage, neck movements, venous puncture, etc.); (e) the recovery

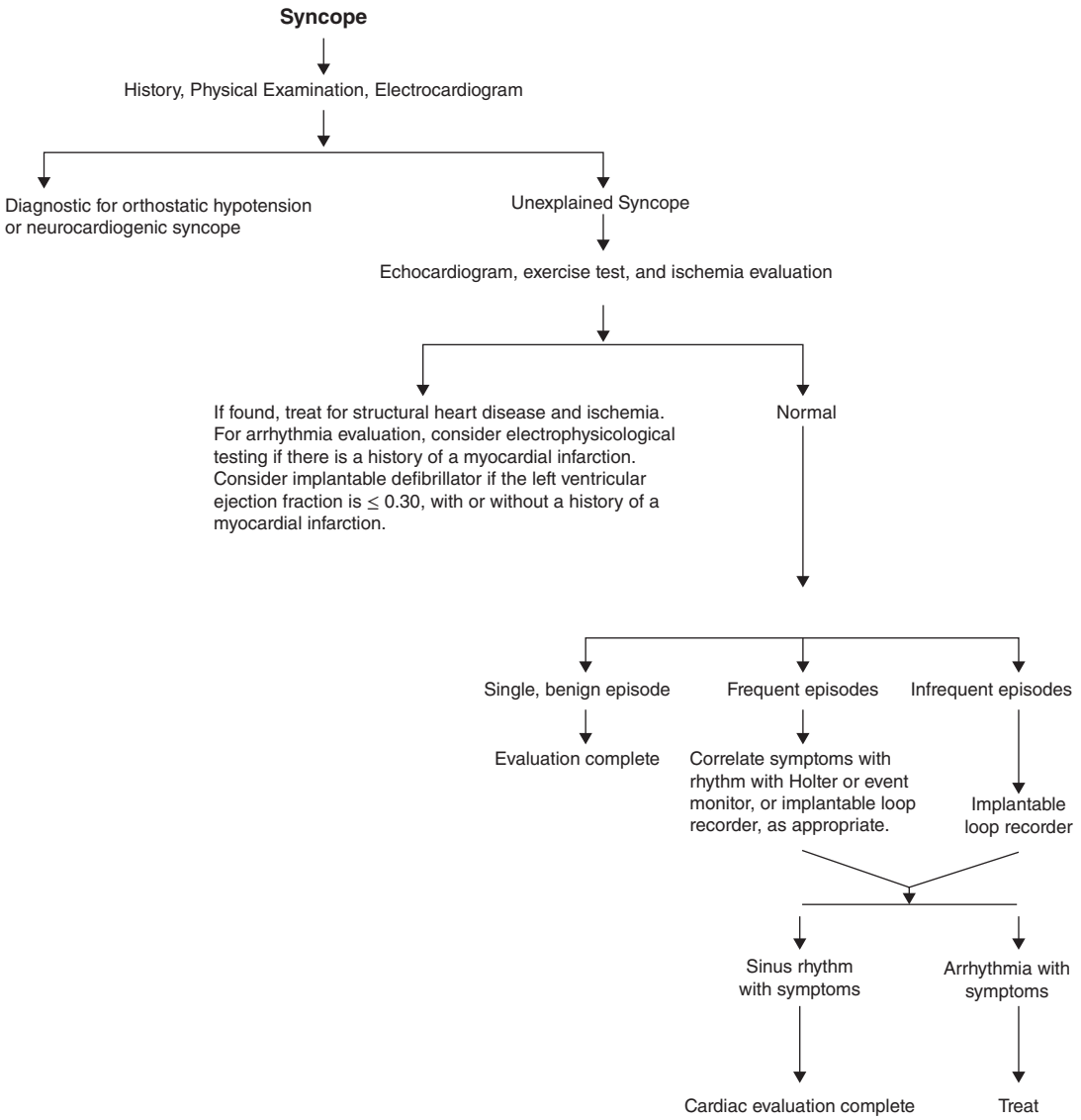

Figure 1.12 Algorhythm for the management of patients with syncope (see text).

of consciousness (rapid or gradual); (f) associated events (tongue biting); and (g) appearance (pallor), and so on.

- With all the data it will be possible, in many cases, to have already an impression of the etiology of syncope. Obviously, it is very important to proceed to **physical examination** (auscultation of the heart and arteries of the neck, and palpation of the heart and vessels).
  - In addition, **correct interpretation of the ECG** is of the utmost importance, particularly AV or bundle blocks, LVH, Q waves, and so on, the correct measurement of the QT interval, and the recognition of possible ECG Brugada patterns, as well as the slight alteration of repolarization seen in V1–V3 that may be considered normal variant but correspond to different inherited heart diseases (see Chapter 9).

Neuromediated syncope usually occurs at rest, although some exceptions exist (see later), with a tendency to occur in standing position or after digestion. Three types of response can be observed during a tilt test (see Appendix A-3, Tilt Table Test): vasodepressor, cardioinhibitory, and mixed. In general, the vasodepressor component is predominant over the cardioinhibitory type (especially in the young and in the very elderly). However, on some occasions, long pauses corresponding to malignant vagal syncopes can be observed. Profund cardioinhibitory responses, including progressive heart rate lowering due to depressed automatism

and/or depressed AV conduction (Figure 1.13), may be life-threatening or contribute to life-threatening situations like motor vehicle accidents. Changes in blood pressure and heart rate are continuously recorded during a tilt test. In the case of significant cardioinhibitory component response, pacemaker implantation may be considered occasionally (see later). Nevertheless, studies using implantable loop recorders demonstrate that even syncope due to serious cardioinhibitory pauses (>15–20 s) do not usually induce permanent cardiac arrest and SD.

Exercise syncope is frequently of cardiac origin and tends to occur abruptly with no prodromal symptoms. Patients may present a Stokes–Adams crisis (see previously). Nevertheless, some syncopes of cardiac origin, including some channelopathies, may often appear at rest. In addition, some exercise syncope may be neuromediated (oftenly in the post-exercise period) (Calkins *et al*., 1995) (see later). It is very important to rule out neuromediated vasovagal syncope in patients with a syncope that occurred during exercise, such as in athletes. However, syncope during exercise is a "red flag" and should prompt immediate actions to determine the cause of syncope. As already stated, **an exercise-provoked syncope is usually associated with a serious structural heart disease**, such as severe aortic stenosis, hypertrophic cardiomyopathy, or acute ischemia or some channelopathies. For this reason, all syncopes presented during exercise should be thoroughly investigated. This includes detailed clinical and family history to search for SD history, ECG during exercise, echocardiography, tilt test, MRI, coronary angiography, and even electrophysiology studies (EPS) and genetic tests, in order to rule out associated pathology. **Usually the continuation of practicing sports is contraindicated, unless the underlying cause can be resolved** (i.e., WPW with rapid atrial fibrillation). If the neuromediated vagal mechanism can be proven, in the absence of structural heart disease and channelopathies, it is not necessary to discontinue sports activity, but it should be performed under careful control (Calkins *et al*., 1995). Some patients may require "extra" studies in order to allow them to compete professionally.

Currently, **some drugs have been tested in patients with vasovagal syncopes** (β blockers, dihydroergotamine, midodrine, fluhidrocortisone, etc.) but no definitive answer to all patients has been established yet (Brignole *et al*., 1992; Sheldon *et al*., 2010). At the same time, pacemakers do not always offer adequate protection (see later). Nonpharmacological treatment, consisting of lifestyle advice (adequate fluid and salt intake is advised and excessive alcohol intake is discouraged) and physical counter pressure maneuvers (leg-crossing, handgrip and arm tensing, etc.) are recommended as the first-line treatment to avoid vasovagal syncope (Van Dijk *et al*., 2006; Brignole *et al*., 2004; Moya *et al*., 2009). Also, autonomic nervous system training, such as a progressively prolonged time in standing position leaning back on the wall, may be useful avoiding neuromediated syncope, and some promising results have been reported (Reybrouck and Ector, 2006). This difficult to undertake therapeutic approach has been validated in a first randomized placebo-controlled trial with

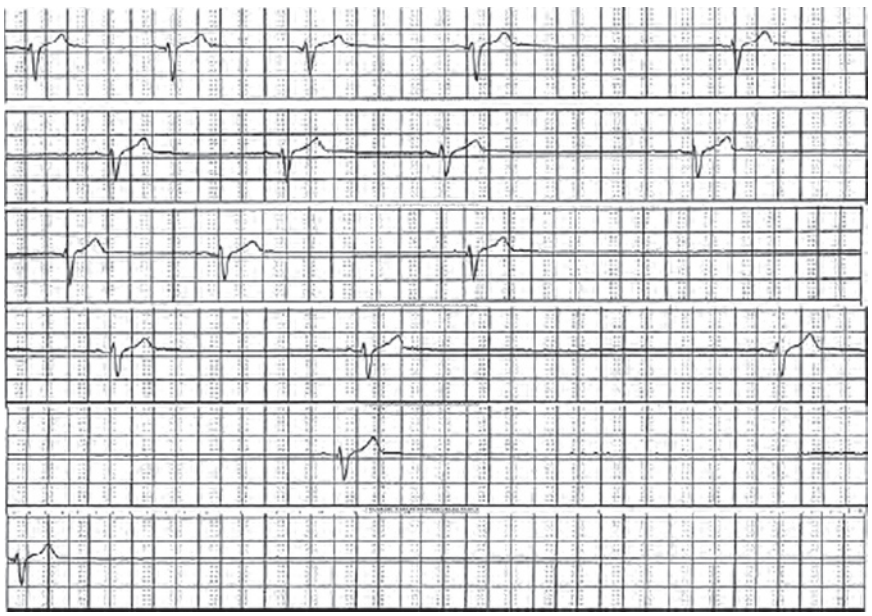

Figure 1.13 Six continuous strips (from a Holter recording) of a patient aged 35 years who presented a syncope after venous puncture. Sinus automaticity is progressively depressed in the absence of an escape rhythm, and a pause lasting 15 s arose leading to syncope.

promising results that hopefully will be confirmed in the future in a larger randomized trial (Tan *et al*., 2010). The authors of this book are not using this approach (tilt training) very much, as most of the patients fail to do it in a systematic manner. It may be used in some doubtful cases and, if positive, help to assume that the syncope is neuromediated.

In orthostatic hypotensive syncope, fluorocortisone may be effective and some drugs (α- and β-blockers, diuretics, angiotensin converting enzyme inhibitors (ACE-I), sublingual nitrates, etc.) should be avoided. It may be beneficial to use long elastic stockings. When spending a long period of time in standing position cannot be avoided, it is advisable to perform the physical counterpressure maneuvers (see before) as a preventive measure to favor venous blood return. It is also helpful to drink plenty of water before prolonged standing position (lectures, etc.). Ideally, one has to avoid and/or control triggering factors, like prolonged standing or venous puncture (Figure 1.13).

Clinical findings suggesting a diagnosis of "syncope" account for around 1% of urgent care clinic visits (see before). Therefore, there is a need for consensus on risk stratification (Benditt and Can, 2010). One of the last proposed is the ROSE rule (Reed *et al*., 2010), which has an excellent sensitivity and negative predictive value (NPV) in the identification of high-risk patients with syncope.

For the management of syncope, we refer to *The Integrated Strategy for Syncope Management* by the European Society of Cardiology (Brignole *et al*., 2004; McCarthy *et al*., 2009; Moya *et al*., 2009). From these guidelines, we will comment on some relevant aspects (Morady 2009):

- Neuromediated and hypotensive syncopes are the most common.
- The examination of a ≥40-year-old patient with syncope must include the compression of the carotid sinus on either side for 10 s. The provocation of pauses of >3 s and/or a decrease in blood pressure of >30 mm is indicative of syncope due to carotid sinus hypersensitivity (see before).
- The tilt test is used to confirm a diagnosis of neuromediated syncope but is not to be used for evaluating the efficacy of treatments. It is acknowledge that proper interrogation may result in fewer tilt tables, reducing costs and diagnostic tests (Sheldon *et al*, 2006, 2010).
- Implantable loop recorders may be more cost effective than external recorders or the conventional Holter recorder in the diagnosis of infrequent syncope (see Appendix A-3, Tilt table test, Figure 1.12). Patients with recurrent unexplained syncope and major structural heart diseases that have received a therapy guided by means of an implantable loop recorder, had a significantly lower number of recurrences (RAST trial) (Krahn *et al*., 2001).
- In patients with syncope and an EF <30%, the implantation of an ICD without prior invasive EPS may be considered. However, in our opinion, neuromediated vasovagal syncope needs to be ruled out in this group of patients. A more complete clinical study is advisable.
- Electrophysiology study may be of help in patients with syncope due to suspected severe bradyarrhythmia (bundle branch block especially with long PR) or history of palpitations (possible associated tachyarrhythmia). Some groups may implant a pacemaker in patients with syncope and bifascicular block. Currently, the group of Shendon in Calgary is running the SPRITELY study, which is randomizing patients with syncope and bifascicular block to receive either an implantable loop recorder or a pacemaker.
- As first-line therapy, to prevent neuromediated syncope, the following measures are advisable: (i) a regular intake of water (minimum of 2.5 liters/day) and salt (2 g/day) unless contraindicated, (ii) the avoidance of triggers (i.e., venous puncture to be standing for long periods of time), (iii) performing muscular contractions in arms and legs, especially standing, (iv) avoiding alcohol, and (v) if prodromal symptoms appear, laying down in dorsal decubitus with the legs raised.
- There is no evidence from any study supporting the efficacy of drugs (β-blockers, disopyramide, midodrine, chloridin, etc.) in preventing neuromediated syncope (see before).
- The usefulness of pacemakers depends on the type of syncope. It is mandatory in the majority of cases of advanced AV block (see Chapter 6, Clinical, Prognostic, and Therapeutic Implications of the Passive Arrhythmia), and also in most cases of sick sinus syndrome and bradycardia–tachycardia syndrome. Obviously, in the majority of cases of VT/VF an ICD has to be implanted. However, **in neuromediated syncope the usefulness of a pacemaker is not universally recommended.** It has even been suggested that the positive results found in some studies may be biased by the placebo effect (Raviele *et al*., 2004). The VPS II Study (Connolly *et al*., 2003), which removed the placebo effect by implanting pacemakers to patients with neuromediated syncope and comparing ON and OFF groups, demonstrated that pacemakers are not useful for the treatment of neuromediated syncope. However, since the INVASY trial (Occhetta *et al*., 2004), it is thought that physiologic pacing starting early, when the decrease in heart rate is detected (e.g., using a Medtronic VERSA), may help to

avoid syncope from recurring. Some patients with profound cardioinhibitory syncope may benefit from pacemaker implantation. In those cases, "rate-drop" pacemakers (Medtronic) are recommended because they can be activated early at the beginning of the pause, avoiding the patient to become symptomatic. Finally, in patients with hypersensitive carotid sinus syncope, implantation of bicameral pacemaker has been shown to be effective (Kenny *et al.*, 2001).

- The occurrence of a recent (i.e., within the last 6 months) unexplained syncope in patients with hypertrophic cardiomyopathy is a risk factor for SD (see Chapter 9, Hypertrophic Cardiomyopathy).

Arrhythmias and Unpleasant but not Serious Symptoms

Many active arrhythmias, whether isolated (premature atrial or ventricular complexes) or sustained (atrial fibrillation, tachycardias), do not result in evident hemodynamic disturbances but are subjectively uncomfortable, appearing in the form of precordial discomfort, regular or irregular palpitations (to feel the heart beat), and dyspnea. The sensation of anticipated beats is typical for premature complexes, whereas fast regular or irregular palpitations suggest paroxysmal tachycardias or atrial fibrillation, especially if the onset is sudden. A sensation of very rapid neck pulsations is typical for paroxysmal AV junctional reentrant tachycardia (see Chapter 4, Junctional Reentrant (Reciprocating) Tachycardia: Clinical Presentation). In contrast, sinus tachycardia is characterized by regular, gradually increasing palpitations. Also, nonsevere bradyarrhythmias may induce dizziness and fatigue, especially if the heart rate does not increase properly with exercise.

The patient may be concerned about these symptoms, but they usually do not represent a severe concern. However, this does not mean that they are not potentially dangerous symptoms and that no treatment has to be prescribed. It will depend essentially on the patient's clinical context.

Asymptomatic Arrhythmias

Finally, there are other cases in which the patient may be unaware of the presence of an arrhythmia, including frequent PVCs or relatively rapid atrial fibrillation. It should be borne in mind that, in general, PVCs are detected more easily in healthy subjects than in subjects with severe heart disease. However, it could be necessary to treat these arrhythmias if prognosis could be improved. The presence of asymptomatic PVCs with special characteristics are markers of risk in many cases, such as post-MI (Bigger *et al.*, 1984; Moss *et al.*, 1979), HF (Van Lee *et al.*, 2010) hypertrophic CM (McKenna *et al.*, 2002), and other inherited heart diseases, and so on., and sometimes need to be treated (see Chapters 5, 9 and 11). Some passive arrhythmias, such as severe bradycardia, second-degree Wenckeback type AV block in athletes, or vagal overdrive, may be completely asymptomatic, and usually do not require specific treatment (see Chapter 6, Clinical, Prognostic, and Therapeutic Implications of the Passive Arrhythmia).

The Importance of Clinical History and Physical Examination in Diagnosis and Assessment of Arrhythmias

(Bellet, 1969; Knoebel et al., 1993; Recommended General Bibliography p. xvii)

It must be remembered that it is not an electrocardiographic tracing with a heart rhythm disorder that is being dealing with but a patient with a special clinical context who presents an arrhythmia. History taking and physical examination will help us to determine the type of arrhythmia with which we are dealing and to make an overall assessment based on the following facts:

- An arrhythmia may or may not be suspected before an ECG is performed. Sometimes a patient describes a change in heart rhythm suggestive of an arrhythmia, but nothing appears on the ECG tracing, even if an arrhythmia is detected during the physical examination. These cases need complementary testing (an exercise test, and especially a Holter ECG recording) for a clear diagnosis and evaluation. Alternatively, it may be possible to detect an arrhythmia during a physical examination when the patient does not present any suggestive symptoms.
- Bear in mind that the prognostic importance and the therapeutic implications of arrhythmias depend to a large extent on the clinical setting in which they occur.
- Moreover, there are special situations (athletes with syncope, patient's relatives with a history of SD) in which it becomes important to integrate the family history, physical examination results, and surface ECG with other special electrocardiographic techniques (exercise testing, Holter ECG recording, EPS) and imaging techniques (echocardiography, cardiac MRI, and coronarography), as well as genetic tests, to reach a correct diagnosis, to determine the patient's prognosis, and to be able to take the most appropriate therapeutic decision. It is important to emphasize the value of extensive electrocardiographic knowledge, as minor

changes (i.e., repolarization abnormalities), such as the presence of negative T waves in leads V1 to V3–V4 in the case of arrhythmogenic right ventricular dysplasia, or a slight ST-segment elevation with r′, usually seen in lead V1 in the case of Brugada syndrome, may be essential to suggest a diagnosis.

Management of a Patient with Suspected Arrhythmias

In order to make a diagnosis of arrhythmia, two factors in particular should be taken into consideration by a physician when examining a patient: (i) the rate of the heart rhythm and (ii) heart rhythm regularity or irregularity.

The study of these two characteristics of the heart rhythm through history taking and physical examination (especially arterial pulse palpation and auscultation) is very important for the presumptive diagnosis of arrhythmias, even though electrocardiography remains the definitive and key technique for such diagnoses. It should be emphasized that the arrhythmia should not be viewed as an isolated ECG recording, but as a tracing taken within a given clinical setting.

History Taking

The patient may present symptoms: palpitations, dyspnea, angina, dizziness, or syncope (Stokes–Adams attack). However, it is advisable to remember that the patient is often not aware that they present any type of arrhythmia. Sometimes, not only does the patient not take notice of the onset of arrhythmia, but they are also not aware of the presence of a rapid/slow, regular/irregular rhythm. This happens particularly in atrial fibrillation with relatively slow rates and in many cases of premature complexes. If the patient feels the arrhythmia, history taking and the physical examination will inform if isolated irregularities of the pulse, typical of premature complexes, are present, or if regular or irregular episodes of rapid or slow rhythm are present.

The onset of an episode in a patient with a rapid heart rate may be progressive (sinus tachycardia) or sudden, from one second to the next (paroxysmal tachyarrhythmia). When tachycardias appear and disappear in a sudden but repetitive way, they are called incessant tachycardias. It should be noted that a characteristic of supraventricular paroxysmal tachycardias is that not only are the onset and cessation abrupt (paroxysmal), but also polyuria may occur at the end if the episode is long. In the presence of a paroxysmal AV junctional reentrant tachycardia (AVJRT), with the circuit exclusively in the AV junction (AVNRT), the patient may feel a rapid regular pounding in the neck due to the transmission of atrial activity contracting against the closed AV valves. This does not happen when an accessory pathway participates in the reentry circuit (junctional reentrant tachycardia with accessory pathway (AVRT)) (see Chapter 4, Junctional Reentrant (Reciprocating) Tachycardia).

In fact, the feeling that the heart beat exist is the demonstration that the heart contraction is strong and presumably in a failing heart usually the presence of strong contraction is not frequently felt. Patients with acute AM present frequently PVC but often are not aware of that.

The Physical Examination

The physical examination (especially palpation and auscultation) obviously allows the heart rate to be checked and determines whether the rhythm is regular or irregular (see above).

It may also be useful to verify the presence of AV dissociation (atria and ventricles contract separately and independently). The presence of AV dissociation practically ensures that a wide QRS complex tachycardia is of ventricular origin (AV dissociation by interference). If the rhythm is slow, it corresponds to an advanced AV block (AV dissociation by block). In these cases, the first heart sound varies in intensity in accordance with the relationship between the P wave (atrial contraction) and the QRS complex (ventricular contraction) (Figure 1.14).

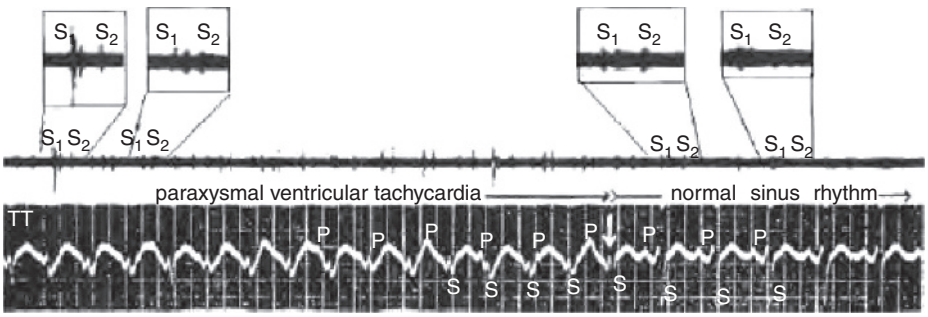

Figure 1.14 Differences in the intensity of the first heart sound during a ventricular tachycardia (VT). Note how, when it reverts, after quinidine administration, the intensity of the first sound is unchanged (Bellet, 1969).

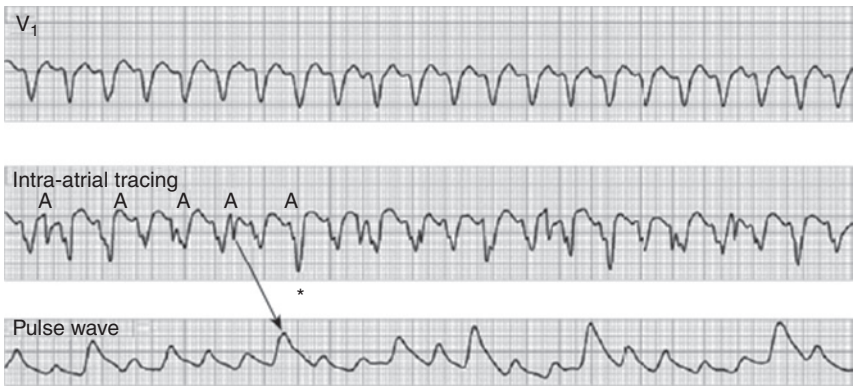

Figure 1.15 Ventricular tachycardia with atrioventricular (AV) dissociation. The dissociation between atrial (A) and QRS complexes is very evident in the intra-atrial tracing. Furthermore, when the A wave precedes the QRS, the AV synchrony provokes a vigorous pulse wave (arrow). Meanwhile, when the A wave overlaps with the QRS, the pulse wave is weaker, yet the contraction against closed AV valves causes a cannon wave in the intra-atrial recording (asterisk).

Be reminded that the AV valves open with the atrial contraction (P wave), and the first heart sound is recorded when the AV valves close. A long P-QRS interval means that the first heart sound has been generated at the time that the leaflets of the AV valve are nearly closed, as a long time has passed since the atrial contraction, and they tend to get back to this previous position spontaneously. Therefore, when closing, no intense heart sound may be detected. Meanwhile, if the closure happens immediately following the atrial contraction, the leaflets of the AV valves are separate and the first heart sound is louder. Thus, in AV dissociation, when the P-QRS interval is short, the first heart sound is more intense, like cannon shot (Bellet, 1969). In practice, AV dissociation produces a first heart sound of varying intensity in the clinical auscultation (Figure 1.14).

The presence of cannon A waves (A wave of high amplitude) in the venous pulse, which occurs when the atrial and the ventricular contractions eventually coincide, and the verification of variable systolic pressure may also help to diagnose AV dissociation (Figure 1.15).

Monitoring and recording of the venous pulse, blood pressure monitoring, and especially auscultation of the first sound may help to make a diagnosis of atrioventricular (AV) dissociation.

These classical signs may still be useful to make a differential diagnosis between ventricular and supraventricular tachycardia with aberrancy, and to suspect an advanced AV block when bradyarrhythmia is present. Undoubtedly, when the patient is in critical condition, the most important thing is to give therapeutic assistance as soon as possible.

Today, data obtained from the physical examination in a patient with arrhythmia are scarcely used as a diagnostic tool, because they are difficult to obtain and to record, and an ECG, which is the key tool for diagnosis, may be performed immediately at any medical center. However, it will be of interest to readers to know that, as just stated, the auscultation of the first heart sound (Figure 1.14) may be useful for a differential diagnosis of wide QRS complex tachycardia and slow rhythms (sinus bradycardia vs advanced AV block). In patients with regular tachycardia and a wide QRS of uncertain origin, the usefulness of the physical examination, so well studied in the nineteenth century by McKencie and Wenckebach, in particular the auscultation of the first heart sound and the examination of the venous pulse, has been confirmed (Garrat *et al*., 1994).

Arrhythmias may be suspected after history taking or physical examination in any of the following circumstances:

- Subjective feeling of heart rhythm anomalies (regular or irregular palpitations, anticipated beat, etc.).
- History of episodes of tachycardia characterized by abrupt onset, sometimes with pounding in the neck, and concomitant polyuria.
- Dizziness with slow or very rapid rhythm.
- Past history of pre-syncope or syncope, even without knowledge of coinciding heart rhythm disturbances.
- Irregular or very slow (<40 bpm) or rapid (>100 bpm) heart rhythm, even in the absence of symptoms.
- Any transient variation in the intensity of the first sound at auscultation, in the amplitude of venous pulse A wave, and in the blood pressure levels.
- Absence of changes in heart rate during exercise, or during the day and night.
- Abrupt changes in heart rate from one beat to the next.

The Importance of Surface ECG and Other Techniques

Surface ECG recording is the key technique used for diagnosis of a cardiac arrhythmia. Carotid sinus massage with electrocardiographic recording may help in the differential diagnosis of the different types of tachyarrhythmias, according to the results of this maneuver (Figures 1.16 and 4.70) (Table 1.4).

On some occasions, however, conventional surface electrocardiography cannot confirm an arrhythmia suggested by history taking or physical examination, or it cannot confirm the correct diagnosis. In searching for the arrhythmia, some other tests have to be used (Holter ECG recording, event loop recorder, exercise ECG testing, tilt test, etc.). To reach the correct diagnosis, it may be necessary to perform intracavitary EPS or use amplified waves (Bayés de Luna, *et al*., 1978) and filtering systems (Goldwasser *et al*., 2011), which are not available in commercial devices. Through these latter techniques, it is possible to see the P wave or ectopic atrial activity when it is not visible or is hidden in the precedent T wave (see Appendix A-3, Other Surface Techniques to Register Electrical Cardiac Activity, Figures A.13 and 4.62). It will also sometimes be necessary to have radiologic and echocardiographic data, as well as other imaging techniques (isotopes, MRI), coronarographic studies (conventional and/or noninvasive), and even genetic tests to determine the presence of associated diseases and to be able to better assess the prognosis of the arrhythmias (see Appendix A-3, Other Nonelectrocardiographic Techniques).

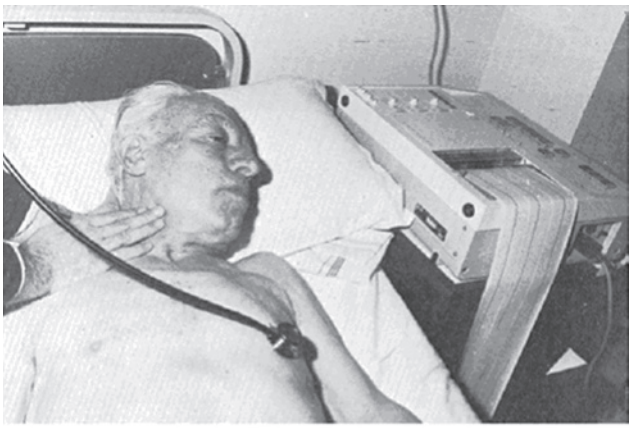

Figure 1.16 Note the correct procedure for carotid sinus massage (CSM). The force applied with the fingers should be similar to that required to squeeze a tennis ball, during a short time period (10–15 s), and the procedure should be repeated four to five times on either side, starting on the right side. Never perform this procedure on both sides at the same time. Caution should be taken in older people and in patients with a history of carotid sinus syndrome. The procedure must include continuous ECG and auscultation. (A–E): examples of how different arrhythmias react to CSM. See Table 1.4 for more information.

Table 1.4 Response of the different arrhythmias elicited by carotid sinus massage (CSM).

Arrhythmia	Response
1. Sinus tachycardia	Without evident effect on the tachycardia, but appears to cause a transient slowing down. If the mechanism is reentry, no changes are observed
2. Monomorphic focal atrial tachycardia	Depends on mechanism: without effect if the mechanism is micro-reentry; sometimes transitory suppression if occurs by increased automatism; frequently suppression if by triggered activity
3. AV junctional tachycardia due to an ectopic focus	Without effect on the tachycardia
4. AV junctional reentrant tachycardia (AVJRT)	The tachycardia can finish. If not tachycardia continues without changes in the heart rate
5. Atrial fibrillation	Without effect on the fibrillation rate, but there is a slowing down of the ventricular rate due to AV block
6. Atrial flutter (including the atrial macro-reentrant tachycardia)	Without effect on the arrhythmia, but frequently more atrial waves are blocked by vagal action on the AV node. This is useful when the atrial waves are not visible.
7. Ventricular tachycardia	In general, without effect on the arrhythmia. However, exceptionally, some cases of ventricular tachycardia have stopped with vagal maneuver

Electrocardiographic Diagnosis of Arrhythmias: Preliminary Considerations

To make a valid electrocardiographic interpretation of an arrhythmia and understand the electrophysiologic mechanism that may explain its presence, it is necessary to take into account the following:

- It is advisable to have a magnifying glass and calipers (alternatively, the use of available commercial semi-automatic calipers, i.e., ICONICO, USA). They may be used to accurately measure the wave duration, the distance between P waves or QRS complexes, the differences in the coupling interval (distance between a premature P wave or QRS complex and the P wave or QRS complex of the preceding basal rhythm), and so on. With current digitalized ECGs saved as PDF files: magnification ×8 or ×10 is also beneficial.
- It is helpful to take a long strip of the ECG tracing, especially important in the case of possible parasystole, and record 12-lead ECGs. This will help to perform the differential diagnosis of ventricular versus supraventricular tachycardias with aberrancy, and also will help to determine the site of origin and mechanisms of supraventricular and ventricular arrhythmias.
- In the case of paroxysmal tachycardias, a long strip should be recorded during carotid sinus massage, and some maneuvers (deep respiration and Valsalva, as well as other vagal maneuvers) performed for diagnostic and therapeutic purposes (Figures 1.16 and 4.70, Table 1.4).
- It is advisable to obtain ECG recordings during exercise testing, both in patients with premature complexes, in order to verify if they increase or decrease, and in patients with bradyarrhythmias, to identify an abrupt or gradual acceleration. If acceleration is abrupt, and the heart rate is doubled or even more, this indicates a 2:1 sinoatrial block. If acceleration is gradual, this indicates a bradycardia due to depression of automatism.
- It is useful to have the overall patient history and previous ECGs. This is especially necessary in patients with potential pre-excitation syndrome or in patients with wide QRS complex tachycardias.
- **The "secret" to making a correct diagnosis of arrhythmia is to properly detect and analyze the atrial and ventricular activity and to determine the AV relationship**. For this purpose, over 90 years ago (Johnson and Denes, 2008), Lewis created some diagrams that are still considered very useful today. In most cases, only three areas are required to explain the site of onset and the stimulus pathway: atria, AV junction, and ventricles (Figures 1.17 and 1.18). Figure 1.19 shows how to outline Lewis diagrams in order to define the AV relationship.
- It is advisable to **determine the sensitivity, specificity, and predictive value of the different signs and diagnostic criteria**. This is especially important when performing differential diagnosis in the case of wide QRS tachycardia, between ventricular tachycardia and supraventricular tachycardia with aberrancy (see Appendix A-2).
- As previously stated, **it is often necessary to perform special techniques**, such as exercise testing, Holter ECG recording, amplified waves, EPS, imaging techniques, etc., to better understand the prevalence of arrhythmias, the electrophysiologic mechanisms that may explain them, and the correct diagnosis, as well as for prognostic evaluation and the prescription of a particular treatment. Appendix A-3 briefly presents all these techniques.

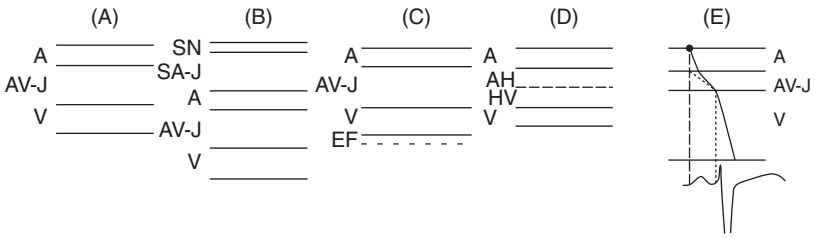

Figure 1.17 A, B, C and D: several examples of Lewis diagrams including: (A) only the atrioventricular (AV) junction, (B) the AV and sinoatrial (SA) junctions, (C) a ventricular arrhythmogenic focus, and (D) a division of the AV junction in two parts, (AH–HV). (E) it depicts the way of the sinus impulse (•) through the atria and AV junction as per the diagram shown in (A). The solid line shows the real way of the impulse across the heart. In general the dashed line is used instead, because it is the place at which the atrial and ventricular activity starts. Thus, the time that the sinus impulse spends to arrive and to cross the AV junction, the most important information, is more visible. EF: ectopic focus.

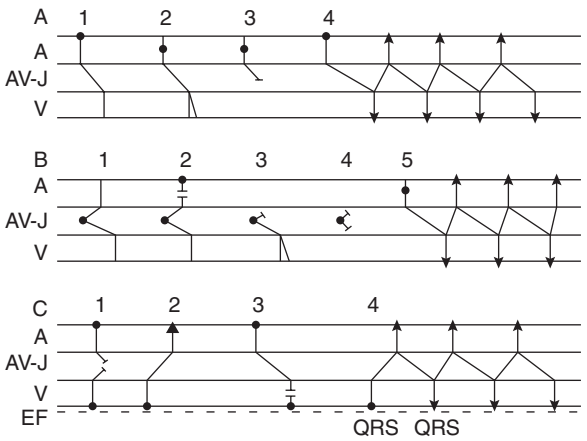

Figure 1.18 (A): 1: normal atrioventricular (AV) conduction of sinus impulse; 2: premature atrial impulse (complex) with aberrant ventricular conduction; 3: premature atrial impulse blocked at the AV junction; 4: sinus impulse with slow AV conduction that initiates an AV junctional reentrant tachycardia. (B): 1: premature junctional impulse with an anterograde conduction slower than the retrograde; 2: premature junctional impulse sharing atrial depolarization with a sinus impulse (atrial fusion complex); 3: premature junctional impulse with exclusive anterograde conduction and, in this case, with aberrancy (see the two lines in ventricular space); 4: premature junctional impulse concealed anterogradely and retrogradely; 5: premature atrial impulse leading to AV junctional reentrant tachycardia. (C): 1: sinus impulse and premature ventricular impulse that cancel mutually at the AV junction; 2: premature ventricular impulse with retrograde conduction to the atria; 3: sinus impulse sharing ventricular depolarization with a premature ventricular impulse (ventricular fusion beat); 4: premature ventricular impulse triggering an AV junctional reentrant tachycardia. EF: ectopic focus.

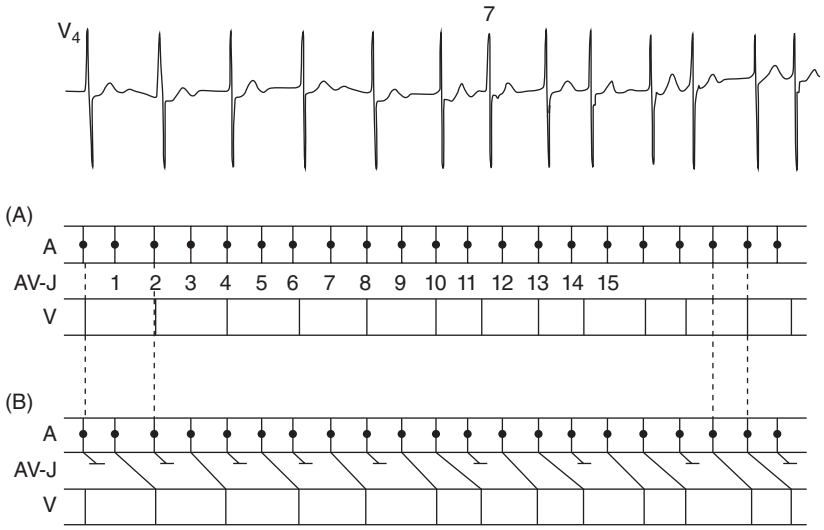

Figure 1.19 Placement of atrial waves and ventricular waves within the atrial and ventricular spaces, as seen at first glance (A). Although at first glance we do not see two atrial P waves for each QRS, we presume that atrial waves are ectopic (negative in V4 and probably very fast), and have to be double the QRS complexes, one visible and the other hidden in the QRS. This is confirmed when we check carefully the bigeminal rhythm. Later on we joined the atrial and ventricular waves through the AV junction (B). These data come from a patient with cardiomyopathy and digitalis intoxication, showing an atrial rate of 150 bpm and a first ventricular rate of 75 bpm. Later on, there are coupled bigeminal complexes. This is an example of ectopic atrial tachycardia with 2×1 AV block and later Wenckeback 3×2 AV block. The atrial waves are ectopic because their morphology differs from sinus P waves seen in previous ECG, and because it is very narrow (0.05 s) and negative in V4. The digitalis intoxication explains the presence of AV block. The first, third, fifth, seventh, and ninth P′ waves conduct with long PR interval (0.40 s). The seventh QRS complex (7) is premature and precedes a series of coupled complexes (bigeminal rhythm). This complex is probably not caused by the eleventh atrial wave, as the corresponding P′R lasts only 0.18 s, whereas the other previous conducted atrial waves (P′), with the same coupling interval, show a P′R of 0.40 s. Instead, the tenth atrial wave (P′) may be conducted with a P′R of 0.56 s; and therefore the eleventh P′ is not conducted. The sequence: P′R = 0.40 s, P′R = 0.56 s, P′ not conducted is afterwards repeated, perpetuating the Wenckebach sequence where the twelfth and thirteenth P′ waves are conducted, whereas the fourteenth is not, etc.

Self Assessment

A. What is an arrhythmia?
B. How are arrhythmias classified in this book?
C. What is the essential significance of arrhythmias?
D. What are the diseases most frequently associated with sudden death (SD)?
E. What are the final arrhythmias preceding SD?
F. How can we identify subjects at high risk for SD?
G. How can SD be prevented?
H. Describe the most important mechanism of syncope.
I. Describe the first-line measures to prevent neuromediated syncope.
J. Why does the first sound vary in intensity?
K. When may an arrhythmia be suspected after history taking and physical examination?
L. What are the previous considerations to be taken into account when making a diagnosis of arrhythmia?
M. What are the Lewis diagrams?

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