

# Pacemakers: where is the block?

Pacemaker implantation has become routine in the management of bradycardia and remains its only safe treatment, having an enormous evidence base of prognostic and symptomatic benefits. Over 565,000 pacemakers are implanted worldwide each year but the rate is half the European average in the UK. **Dr Chris Plummer** explains many elderly people that would benefit from a pacemaker are not being identified.

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**A**rne Larsson was born on 26 May 1915. At the age of 43 he was diagnosed with a fatal disease – complete heart block with Stokes-Adams attacks. His wife would not accept her husband’s inevitable death and, having heard of animal experiments with cardiac pacing, she persuaded a surgeon, Åke Senning from the Karolinska Institute, and an engineer, Rune Elmqvist, who worked for a medical electronics firm in Stockholm, to build (in Elmqvist’s kitchen) and then implant, the first human pacemaker on 8 October 1958<sup>1</sup>.

Arne Larsson died at the age of 86 on 28 December 2001, 43 years, 22 pacemakers and five electrode systems later, from an unrelated malignancy.

Pacemaker implantation is the only safe treatment for bradycardia. We now take this remarkable technology for granted. We have extremely reliable, safe, cost-effective devices with an enormous evidence base of improving symptoms and prognosis. Yet pacing is greatly underused in the UK, with implant rates far below those in our neighbouring European countries [Fig 1]<sup>2</sup>. Because the need for pacing is so closely associated with age [Fig 2], this is an important elderly care issue which must be addressed if we are to give our patients the standard of care they deserve.

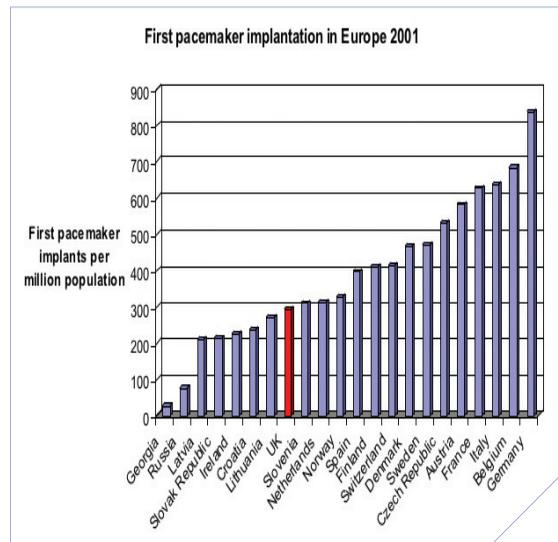


Fig 1. European pacemaker implantation rates in 2001. Data from the world survey of cardiac pacing and cardioverter-defibrillators<sup>2</sup>.

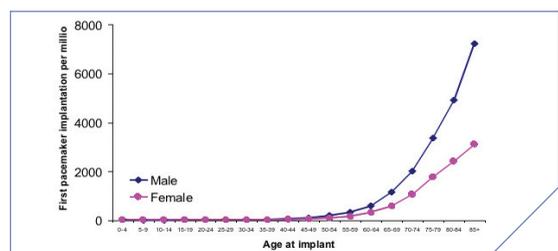


Fig 2. First pacemaker implants per million population in England in 2003-4 against age at implant.

\*AD Cunningham, personal communication, 2006.

## Background

Contraction of the heart, like all muscle, is co-ordinated by electrical impulses. Unlike skeletal muscle, however, the heart receives only tonic neural input which comes from sympathetic and parasympathetic nerves. The precise co-ordination of myocardial contraction is controlled by specialised muscle cells in the walls of the heart itself.

## Impulse formation

The heart rate is controlled by the least electrically stable tissue in the heart. This is normally the sinoatrial (SA) node, a cluster of specialised myocytes high in the right atrium. Intracellular recordings have shown spontaneous depolarisation during diastole (phase 4 depolarisation) in these pacemaker cells controlled by the *If* current [Fig 3]<sup>3</sup>. The slope of this depolarisation, and thus the heart rate, is increased by adrenergic stimulation from sympathetic nerves or circulating catecholamines, and decreased by acetylcholine from vagal input.

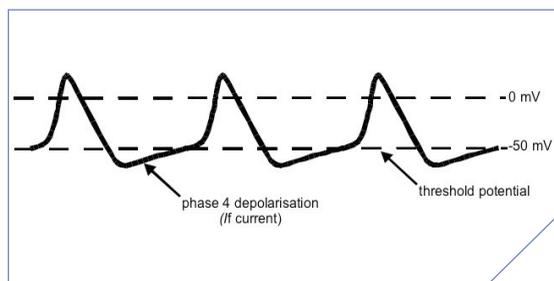


Fig 3. Intracellular potentials in sino-atrial node cells showing diastolic depolarisation.

## Impulse conduction

From the SA node, impulses travel through the atrial myocardium, resulting in atrial systole expelling blood into the ventricles. When an impulse reaches the atrio-ventricular (AV) node at the top of the interventricular septum it is delayed by 120 to 200ms (the normal PR interval) allowing time for ventricular filling before the impulse is conducted to the His bundle, down the bundle branches and into the Purkinje system.

Because these specialised conduction tissues conduct impulses at high velocity through gap junctions, this results in rapid ventricular contraction, a narrow QRS complex ( $\leq 120$ ms) on

the surface electrocardiogram (ECG) and an efficient co-ordinated ventricular contraction [Fig 4]. Another important property of the AV node is that as it is presented with increasingly rapid inputs, these are increasingly delayed (decremental conduction) until, at the Wenckebach point, an increasing proportion are blocked from reaching the ventricles. This prevents the very rapid ventricular stimulation, which would otherwise occur in atrial fibrillation (AF) from inducing ventricular fibrillation.

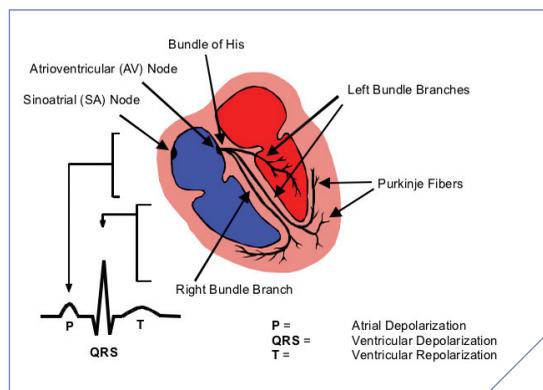


Fig 4. Specialised conduction tissue of the heart showing the surface ECG.

## Failure of impulse formation

If spontaneous SA node depolarisation slows inappropriately or fails completely, another focus within the atria – the atrio-ventricular (AV) node – the His bundle, one of the bundle branches or the ventricular myocardium itself will take over this intrinsic pacemaker function in a series of ‘fail-safe’ mechanisms. This results in bradycardia at rest or the failure of heart rate to increase appropriately on exercise – sinus node dysfunction (SND).

SND is associated with fibrosis and loss of pacemaker cells. This process is associated with age, but the cause is often unknown with only occasional evidence of direct infiltration with malignancy, inflammatory disease, cardiomyopathy, ischaemic or direct surgical damage.

The rate of SA node depolarisation is reduced by high vagal tone, as seen in highly trained athletes, and neuro-cardiogenic reflex syncope. Other medical conditions such as hypothyroidism, elevated intracranial pressure, obstructive jaundice and hypothermia depress sinus node function as do beta-blockers ( $\beta$ -blockers), rate-limiting calcium

antagonists, lithium and the new *If* blocker, ivabradine.

### Failure of impulse conduction

Delayed conduction through the AV node (shown by a PR interval of >200ms) represents first degree heart block. While this is often asymptomatic, it can reduce cardiac output as there is often mitral and tricuspid regurgitation before ventricular contraction. In second degree heart block, not all impulses are conducted to the ventricles. In type 1 there is a progressive lengthening of the PR interval before a non-conducted P wave (Wenckebach) while in the type 2 form, there is a fixed PR interval in the conducted beats with non-conducted beats usually in a 2:1 or 3:1 ratio. Complete failure of AV conduction is known as third degree heart block. Depending on the escape rhythm, this can be relatively asymptomatic or result in syncope or even sudden cardiac death.

Failure of conduction in one or more the bundle branches results in the delayed contraction of the ventricular wall it supplies as the impulse has to spread through normal myocardium rather than the specialised conduction tissue. This results in the broad QRS complex seen on the surface ECG. In people with normal ventricular function, this is usually asymptomatic, but in those with impaired function, any loss of co-ordination between the medial (septal) and lateral walls of the left ventricle can cause or worsen heart failure.

Conduction tissue fibrosis is the most common cause of heart block in older adults. It can also be associated with aortic valve stenosis or ischaemic damage. Drugs that affect AV node conduction include  $\beta$ -blockers, rate-limiting calcium antagonists and digoxin, which acts predominantly by augmenting vagal tone.

### Pacemakers

Pacemaker technology has evolved rapidly from its beginnings in the 1950s. Devices have become smaller and increasingly sophisticated [Fig 5]. Functionally, all pacing systems contain one or more leads with electrodes in the heart, connected to battery powered circuitry which senses intrinsic impulses, time intervals between these impulses and can deliver electric pulses to the heart to trigger contraction. Under local anaesthetic, leads are implanted in the heart chambers, usually via the subclavian vein under x-ray guidance. When



Fig 5. Pacemakers

\*With thanks to Medtronic Inc for permission to reproduce this image.

correctly positioned radiographically and electrically, they are attached to the pacemaker pulse generator, which is placed in a 'pocket' fashioned immediately in front of – or occasionally beneath – the pectoral muscle.

The patient is discharged the following day after satisfactory chest x-ray and pacing checks performed by radio telemetry.

Patients are usually followed up at six weeks, six months and then annually until the battery is depleted, usually after seven to 10 years, when they are electively readmitted as a day case for generator replacement.

### Pacemaker nomenclature

Pacemakers are described by a code developed jointly by the UK and US pacing societies<sup>4</sup>. This comprises three initial letters: the first refers to the chamber paced, the second to the chamber where sensing of impulses takes place and the third to the device's response to sensing. The devices most commonly used in the UK are VVI (ventricular pacing, ventricular sensing and inhibition of pacing by sensing), AAI (atrial pacing, atrial sensing and inhibition of pacing by sensing) and DDD (dual chamber pacing, dual chamber sensing and a dual response of inhibition or triggering of ventricular pacing at a programmed interval after atrial depolarisation). An optional fourth letter R refers to rate response, indicating that the device automatically increases the pacing rate on exercise.

### Indications for implantation

Pacemaker implantation is indicated in all those with symptomatic bradycardia without a reversible cause – there is no other safe treatment. The management of those without symptoms is based on

epidemiological data and the results of clinical trials. The common internationally accepted pacing indications are summarised below.

### Pacing for symptoms

Although sinus node dysfunction is the most common reason (26.7 per cent) for pacemaker implantation in the UK<sup>5</sup>, there is little evidence this improves survival – the indication is to improve symptoms. Because these can be relatively non-specific, it is important to correlate symptoms with sinus bradycardia or the failure of heart rate to increase on exercise (chronotropic incompetence), usually by prolonged ECG (Holter) monitoring. In the absence of this correlation, pacemaker implantation can be justified if sinus bradycardia at <40 bpm has been documented. As for sinus node disease, pacemaker implantation is indicated in those with symptomatic AV block at any level without reversible cause. Recurrent syncope due to carotid sinus syndrome is an indication for pacing with a device programmed to treat this form of neuro-cardiogenic syncope<sup>6</sup>.

### Pacing for prognosis

There are conditions where there is good clinical evidence life expectancy is increased by pacing even in the absence of symptoms. These include high degree (third- and second- degree type 2) AV block, those with evidence of widespread conduction system disease (such as alternating left and right bundle-branch block) and those with lesser degrees of AV block (second degree type 1, bi- or tri-fascicular block) where block in or below the His bundle has been demonstrated on electrophysiology study. Further information on pacemaker indications is available in the international guidelines<sup>7</sup>.

### Mode of pacing

The first pacemakers delivered single chamber ventricular pacing only. The development of dual chamber pacing in 1963<sup>8</sup> allowed resynchronisation of atria and ventricles in complete heart block. Although this was clearly an important advance in pacing technology, in most bradycardia patients the magnitude of benefit derived from pacing is far larger than any difference between pacing modes. Evidence from randomised trials suggests that ventricular pacing appears to increase the risk of developing atrial fibrillation<sup>9,10,11,12</sup> and symptomatic heart failure<sup>12</sup> in patients with SND.

In patients paced for AV block, the Pacemaker Selection in the Elderly (PASE) trial<sup>13</sup> and Canadian Trial of Physiologic Pacing (CTOPP)<sup>14</sup> failed to demonstrate any significant difference in mortality or stroke between pacing modes, although the UK Pacing and Cardiovascular Events (UKPACE)<sup>15</sup> study showed ventricular pacing (VVI) was associated with a higher risk of stroke, transient ischemic attack or other thromboembolism (2.5 per cent per year) compared to dual chamber (P=0.04) pacing, which was not different from ventricular rate-responsive pacing (1.7 per cent per year, P=0.93).

In February 2006, the UK National Institute for Health and Clinical Excellence (NICE) issued guidance on pacing mode in symptomatic bradycardia<sup>16</sup>. They recommended dual chamber pacing, except in:

- > patients with SND and normal AV conduction when single chamber atrial pacing is appropriate;
- > in those with continuous atrial fibrillation when single chamber ventricular pacing is indicated; and
- > in those where there are patient-specific factors, such as frailty or the presence of co-morbidities, when the balance of risks and benefits is in favour of single chamber ventricular pacing.

### New pacing indications

Although pacemakers were developed as a treatment for bradycardia, advances in computer technology over the past 40 years have allowed the development of other pacing indications. One of the first was the termination of supra-ventricular tachycardias by high rate atrial pacing. This is now only rarely necessary as most of these tachycardias are cured by catheter ablation, but the same technology is used in implantable cardioverter defibrillators (ICDs) to pace terminate ventricular tachycardia without the need for defibrillation. Many current pacemakers can now store ECGs and intra-cardiac electrograms, allowing diagnosis and then monitoring of the treatment of arrhythmias. With the recognition that atrial fibrillation is strongly associated with SND and that individual paroxysms of AF can be triggered by sinus pauses, algorithms have been developed which suppress these triggers by maintaining a high proportion of atrial pacing.

One of the most interesting developments in pacing over the past decade has been pacing for

## Key points

- > Pacemaker implantation is the only safe treatment of bradycardia and has been shown to be highly cost-effective.
- > Pacing indications increase exponentially with age from midlife.
- > Implantation rates are historically low in the UK compared to other developed countries.
- > Bi-ventricular pacemakers can now improve symptoms in selected patients with heart failure.
- > Increased awareness of pacemaker indications and the appropriate use of investigations will allow us to treat more of our patients with evidence-based device therapy.

heart failure. Many heart failure patients have atrio-ventricular and intra-ventricular conduction delays, especially left bundle branch block, and these can worsen ventricular function by desynchronising contraction. Cardiac resynchronisation devices have been developed to pace the left ventricular free wall via the coronary sinus, and the interventricular septum via the right ventricle. Clinical trials have shown improvements in acute haemodynamic measurements, patient symptoms and, most recently, mortality<sup>17</sup>.

## Where is the block?

Pacemaker implantation improves both quality and quantity of life in appropriate patients, it is highly cost effective, and has recently been endorsed by NICE. Over the past decade the number of devices implanted has increased exponentially around the world, particularly in North America and many European countries, but the UK lags behind most developed countries. We do not yet know the exact sites or causes of this service block, although it appears to be present at all levels, from patients not reporting their symptoms, to under-investigation in primary and secondary care.

It is clear the majority of pacing indications occur in the elderly and that no one should be excluded from pacing for symptomatic bradycardia on grounds of age or cognitive function. We must all consider bradycardia as a cause of our patients' often non-specific symptoms and investigate them appropriately if we are to give them the standard of care they deserve and increase rate of pacemaker implantation in the UK to European standards.

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