Editorial

The pulse in atrial fibrillation

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Science can benefit from challenges to accepted beliefs. On page 4 Rawles and Rowland take issue with two such beliefs,¹ namely: (a) that ventricular rhythm during atrial fibrillation is random; and (b) that in patients with atrial fibrillation the pulse is irregularly irregular. These two aspects of atrial fibrillation should not be confused.

RANDOM VENTRICULAR RHYTHM IN ATRIAL FIBRILLATION

Twenty years ago we decided to study haemodynamic function in patients with atrial fibrillation because we considered that the irregular ventricular rhythm was an experiment of nature in which there was continuous post-extrasystolic potentiation.² We realised that in patients with atrial fibrillation any relation between RR intervals and a haemodynamic variable, for example left ventricular pressure, could be due to an interrelation between the RR intervals themselves. Analysis of the ventricular rhythm in patients with atrial fibrillation³⁻⁶ showed that in most patients with atrial fibrillation the ventricular rhythm was random.

Moreover, the random pattern of the ventricular rhythm during atrial fibrillation was little affected by exercise or digitalis treatment or both.³ Because both are interventions that influence atrioventricular conduction in human beings with sinus rhythm, we concluded that the cause of the random ventricular irregularity lay outside the atrioventricular system. This led to the hypothesis that during atrial fibrillation randomly spaced atrial impulses of random strength reach the atrioventricular node from random directions—a hypothesis that accords well with Moe's multiple wave front theory.⁷ Thus the role of the atrioventricular node in atrial fibrillation was seen as being confined to scaling down the atrial

impulses by refractoriness and concealed conduction.⁸⁻¹⁰

Since this pattern was identified we have studied hundreds of patients by the same computer assisted mathematical technique and have always found a random ventricular rhythm in uncomplicated atrial fibrillation. This was not altered by treatment with various drugs, such as quinidine or verapamil, that are known to affect atrioventricular conduction or in patients with Wolff-Parkinson-White syndrome in which there is anterograde conduction through an accessory tract¹¹ and the atrioventricular node is bypassed.

Others have reported non-random episodes in the ventricular rhythm in patients with atrial fibrillation¹²⁻¹⁴; nevertheless, I maintain that in true uncomplicated atrial fibrillation the ventricular rhythm is random—in other words, it behaves like a genuine renewal process. A new QRS complex may occur between 400 and 2000 ms but its exact timing cannot be forecast. During atrial fibrillation, ventricular extrasystoles may resemble aberrantly conducted atrial impulses^{15 16} and it may be difficult to rule out partial atrioventricular block. Moreover, an average of as few as 237 QRS complexes for each patient as in Rawles and Rowland's paper may easily conceal unwanted errors, especially as they do not provide us with an indication of the accuracy of their measurements.

The World Health Organisation—International Society of Cardiology task force considered that a random ventricular response was a prerequisite of their definition of atrial fibrillation.¹⁷ Nature is not of course influenced by definitions, but it is now generally accepted that the ventricular rhythm is random in patients with atrial fibrillation. There may be exceptions to this rule but I have yet to come across one. If the ventricular rhythm contains non-random episodes or is barely random, this can nearly always be attributed to the circumstances under which the electrocardiographic recording was made.

Arguments about whether or not the ventricular

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rhythm is always random during atrial fibrillation detract from the pathophysiological riddle of why the ventricles behave as they do. Therefore, I am disappointed that Rawles and Rowland, in challenging the existing theory, do not offer an alternative explanation, especially of why the ventricular rhythm was random in 70% of their patients whereas in 30% it was not. They certainly err when they say that the normal distribution of RR intervals cannot be associated with randomly occurring events. The distribution of events and the concept of a renewal process are independent. True, a slight deviation from randomness could be seen in a number of patients in the study reported by Bootsma *et al*,³ but this did not affect the overall conclusions. Although marginal statistical differences should not be ignored, they are not necessarily of biological or clinical importance. So I maintain that for all practical purposes the ventricular rhythm is random in true atrial fibrillation. This is remarkable because most biological phenomena tend to show some predictability or periodicity or both. When the ventricular rhythm in atrial fibrillation is not random one is either dealing with an artefact or a mixture of other arrhythmias or conduction defects or both.

Intra-atrial electrograms obtained during atrial fibrillation show a random and erratic high frequency activation pattern that accords with our original concept of atrial electrical behaviour.^{11 18 19} The arrival of the atrial impulses (at the atrio-ventricular junction) may be mathematically characterised as a Poisson process.¹⁴ It may be difficult to explain non-random ventricular episodes that result from this form of atrial electrical activity, but it is impossible to explain a random ventricular rhythm from a non-random atrial input into the atrio-ventricular junction. Or do Rawles and Rowland suggest that there are three patterns of atrial electrical activity during atrial fibrillation?—one causing a random ventricular rhythm, one responsible for a non-random ventricular rhythm and a negative first order autocorrelation coefficient, and one with a non-random ventricular rhythm and a positive first order correlation coefficient. This is so unlikely that we must seriously question their assumptions. Another disturbing factor is that these three apparently different types of atrial fibrillation are not related to the primary disease that causes or underlies the fibrillation of the atria.

We could only find a reproducible negative first order autocorrelation coefficient in horses with atrial fibrillation and very long RR intervals²⁰ and a predictable positive first order autocorrelation coefficient in patients with atrial fibrillation and high ventricular rates.²¹ For both these exceptions to the rule of randomness we, and others, offered plausible

physiological explanations. These were autonomic interference with atrioventricular conduction in the horse,²⁰ and the short “memory” of the human atrioventricular node.^{6 22} In addition, new findings suggest that the behaviour of the atrioventricular node during atrial fibrillation may be more complicated than originally thought.²³ These findings accord well with the idea that the mammalian atrio-ventricular node, like the sinoatrial node, resembles a biological oscillator.^{14 24 25}

THE IRREGULARLY IRREGULAR PULSE IN ATRIAL FIBRILLATION

Rawles and Rowland misquote¹ my editorial in the *Journal of the American College of Cardiology*.²⁶ I have never stated or taught that the pulse in patients with atrial fibrillation is totally irregular in volume. Indeed in the late 1960s our group removed the dust from Einthoven and Korteweg's neglected paper.²⁷ We demonstrated negative second and higher order cross correlation coefficient(s) between RR intervals and contraction variables in isolated rat hearts during random stimulation.² We also demonstrated, what was later confirmed during clinical investigations, that Starling's law does not explain the variability of the size of the pulse in patients with atrial fibrillation.^{28 29} But it was all there already in Einthoven and Korteweg's paper of 1915.²⁷ The pulse volume in patients with atrial fibrillation is not totally variable.

I think the term “pulsus alternans” during atrial fibrillation is an inappropriate description of fluctuation of the pulse for the following reasons. Pulsus alternans requires that all beats alternate, which is clearly not the case, as can also be seen in Fig. 1 of Rawles and Rowland's paper. Highly specialised computer aided analysis is needed to demonstrate a statistically significant but still rather weak second order cross correlation between RR intervals and ventricular contractile behaviour. In atrial fibrillation with continuously varying RR intervals, short RR intervals potentiate the ventricular contractions whereas long intervals have the opposite effect (depotentialisation).^{2 30} Since short intervals potentiate more than long intervals depotentiate, they do not cancel each other and the net effect is a negative second order cross correlation coefficient.^{29 31} Under clinical conditions the higher order cross correlation coefficients are usually obscured by “noise”. This explains the findings of Rawles and Rowland, but this feature has nothing to do with pulsus alternans. The term “pulsus alternans” should be reserved for regular cardiac rhythms so that its clinical meaning is retained.^{32 33}

I am also concerned that in Figs. 5 and 6 of Rawles and Rowland's paper coefficient 0 in the cross

The pulse in atrial fibrillation

correlograms of RR intervals and stroke distances is statistically significant ($p < 0.01$ and < 0.001 respectively).¹ I find this impossible to accept because the RR interval still lasts while the ventricular contraction takes place, as can be seen in Fig. 7 of Rawles and Rowland's paper. This finding suggests that both RR intervals and left ventricular contractions are determined by a "magic" third factor. The only comment that Rawles and Rowland make about this result is that in Fig. 6 "The cross-correlogram shows a very complex pattern of inter-relations. . .". I wonder whether this unusual finding could be due to the small number of cardiac cycles studied or the disputed stroke distance method that they used.³⁴

I am disappointed that Rawles and Rowland's study does not shed new light on the source of the ventricular irregularity and on its effect on the behaviour of the pulse in patients with atrial fibrillation. But I am grateful for their frank criticism and for this opportunity to respond to it. It made me go over our old data and reflect on our earlier theories.^{2 3 26 35} I have come to the conclusion that as yet we have nothing better to offer and I look forward to further exploration of this fascinating aspect of the study of cardiac arrhythmias.

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