Case Report: Cryptic evidence on underreporting of mRNA vaccine-induced myocarditis in the elderly: a need to modify antihypertensive therapy

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Abstract

Background: Myocarditis has been considered a rare complication of COVID-19 vaccination that primarily affects young people. However, recent studies indicate under-reporting of cases in the elderly. Furthermore, post-mortem studies of five cases (median age 58) that died suddenly within 7 days of vaccination, indicate an autoimmune element. Albeit an individual case history, the author's unexpected personal evidence supports the latter studies.

Methods: Readings of blood pressure (BP) and pulse were taken twice daily.

Results: Seven days after the fifth of a series of anti-COVID-19 vaccinations, a "stress test" (15 min jog) in an elderly subject exposed a cardiac problem – arrhythmia and a rapid fall of BP with slow recovery. The timing suggested myocarditis as a post-vaccination *early* side-effect that usually targets those more likely to exercise (i.e., the young). Thus, it is usually cryptic in the elderly. In addition, retrospective studies of his own BP readings during the vaccination period (2021-2023) revealed the sudden emergence of transient, but prolonged, falls of BP *several weeks* after each of his last four vaccinations. These hypotensive episodes were cryptic (asymptomatic) and likely not detected in shorter post-vaccination analyses.

Conclusions: Short-term post-vaccination side effects are distinct from those occurring after some weeks. The first category includes systemic or localized inflammatory responses that, in the case of the heart, might either trigger arrythmia and acute functional impairment, or remain cryptic. Localized responses could initiate tissue damage, culminating weeks later in the second category – asymptomatic but measurable functional impairment. Continuing regular dosages of antihypertensive medication during this period would likely intensify the hypotension. That this did not occur in the author's case is attributed to his two-decade-long practice of modulating dosage daily, based on BP readings. Failure to follow this protocol might explain some sudden home deaths. A parallel is drawn with his previous study that showed the need to modify antihypertensive therapy in response to external temperature changes.

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Introduction

Citing reports of the US Center for Disease Control (CDC), it was correctly concluded early in the COVID-19 pandemic that most adverse events of vaccination, including myocarditis, "were mild and short in duration".[1] Among these was a 2021 report that myocarditis is more frequent in young versus old, in males versus females and in military males versus non-military males. It was *not* noted that the first mentioned in these pairs tend to exercise more, and that such exercise may reveal cardiac symptoms. However, exercise restriction was recommended for diagnosed cases.[2] An extensive Japanese population study has since concluded that there has been under-reporting of occurrences of myocarditis in the elderly.[3] Furthermore, German biopsy studies[4] and the post-mortems of five subjects (median age 58) that died suddenly at home within 7 days of vaccination,[5] indicate a cardiac autoimmune element.

There is little information on the nature of these sudden deaths. Furthermore, the widely reported "excess deaths" during the period of vaccination, which were not directly attributable to SARS-CoV-2 infection, remain unexplained. Thus, the account of an elderly authority in the field (the present author) of his own exercise-related "near death" experience, 7 days after a fifth ("booster") dosage of an mRNA vaccine, might be helpful. It so happens that he also had available blood pressure (BP) readings for the vaccination period (2021-2023). These readings were part of a two-decade study of the treatment of his own mild hypertension with angiotensin II receptor antagonists (ARBs).[6] The continued use of these has been problematic for COVID-19 patients because they bind the receptor for angiotensin-II (AT_1R) and hence might influence the membrane-associated angiotensin converting enzyme 2 (ACE2), to which the SARS-CoV-2 virus binds.[7][8] The general conclusion has been, either that ARB usage should not influence case management;[9] or that it might help rather than hinder.[10]

However, this paper brings to light circumstances, probably less rare than generally thought, where hindrance is evident. While, through exercising, the author discovered within*days* of vaccination one, otherwise cryptic, cardiac symptom, his retrospectively examined BP readings indicate transient asymptomatic cardiac impairments *several weeks* after the last four of his five vaccinations. This period is much longer than the four-week cut-off employed in some studies,[11] as has recently been noted.[12][13]

He attributes the absence of symptoms (i.e., their crypticity) to his protocol of adjusting ARB doses daily according to BP readings (see proposed novel myocarditis assay in Methods). This practice had previously shown the need to adjust doses according to environmental temperature.[6] As before, the study was carried out with widely available BP monitors. Thus, using a "crowd sourcing" approach,[14] his observations might readily be confirmed by some of the many millions of

hypertensive subjects with a scientific background.

Methods

A BIOS BP and pulse monitor (model BD353; Thermor Ltd., Newmarket, Ontario) was purchased in 2020. The levels and patterns of readings compared well with those of a model from another manufacturer. After resting (>10 min) the author took readings twice daily (approx. 8 am and 8 pm) from his own left arm. According to the results, dosages of antihypertensive agents (Losartan and recently Candesartan) were modulated (zero, half tablet, one tablet, etc.) with the aim of achieving values of 130 and 75 (mm Hg) for systolic and diastolic, respectively.

This protocol was implemented in 2000 when mild hypertension was diagnosed and later facilitated dosage management when BP values were seen to be influenced by environmental temperature.[6][15] While this “time in the therapeutic range” approach is now becoming widely adopted,[16][17] the relative constancy of BP and pulse values means that agent dosages must act as *surrogate* indicators for what the BP values *might* have been. To smooth out random fluctuations, in the present work weekly averages are calculated. For clarity, the author’s results are narrated here in the first person.

Case Description

Post-vaccination acute cardiac arrythmia

Table 1. COVID-19 vaccination schedule and short-term side effects

Date	mRNA vaccine	Side effect (wife)	Side effect	Organ	Post Vaccination Runs
7 Mar 2021	Pfizer	No	No	-	Days 2 and 5
25 June 2021	Pfizer	No	No	-	Days 2 and 8
23 Dec 2021	Moderna	No	No	-	Days 6 and 9
12 May 2022	Moderna	Systemic immune (Day 1)	Local immune	Both Gums Teeth (Day 2)	None
8 Oct 2022	Moderna	Systemic immune (Day 1)	Local immune	Heart (day 7)	Days 3 and 7

In my dotage, my love of running has moderated to 15-minute jogs twice weekly in a nearby park. I continued this after my first three vaccinations with no problems (Table 1). However, after my wife and I had our first “boosters” (fourth vaccination), two widely separated teeth (upper and lower jaws that my dentist had warned were problematic) became very painful. Assuming a local cytokine-release problem (my wife had a systemic one), I did not run. After the second booster (fifth vaccination), I was feeling well and jogged normally on day-3. But 10 minutes into my day-7 jog, I experienced a mild tightening in my chest and sat down. I detected a faint fluttering pulse. Recalling the reported “rare” incidence of postvaccination myocarditis,[1] I assumed atrial fibrillation and walked slowly home where I rested for a while

and then took BP and pulse readings.

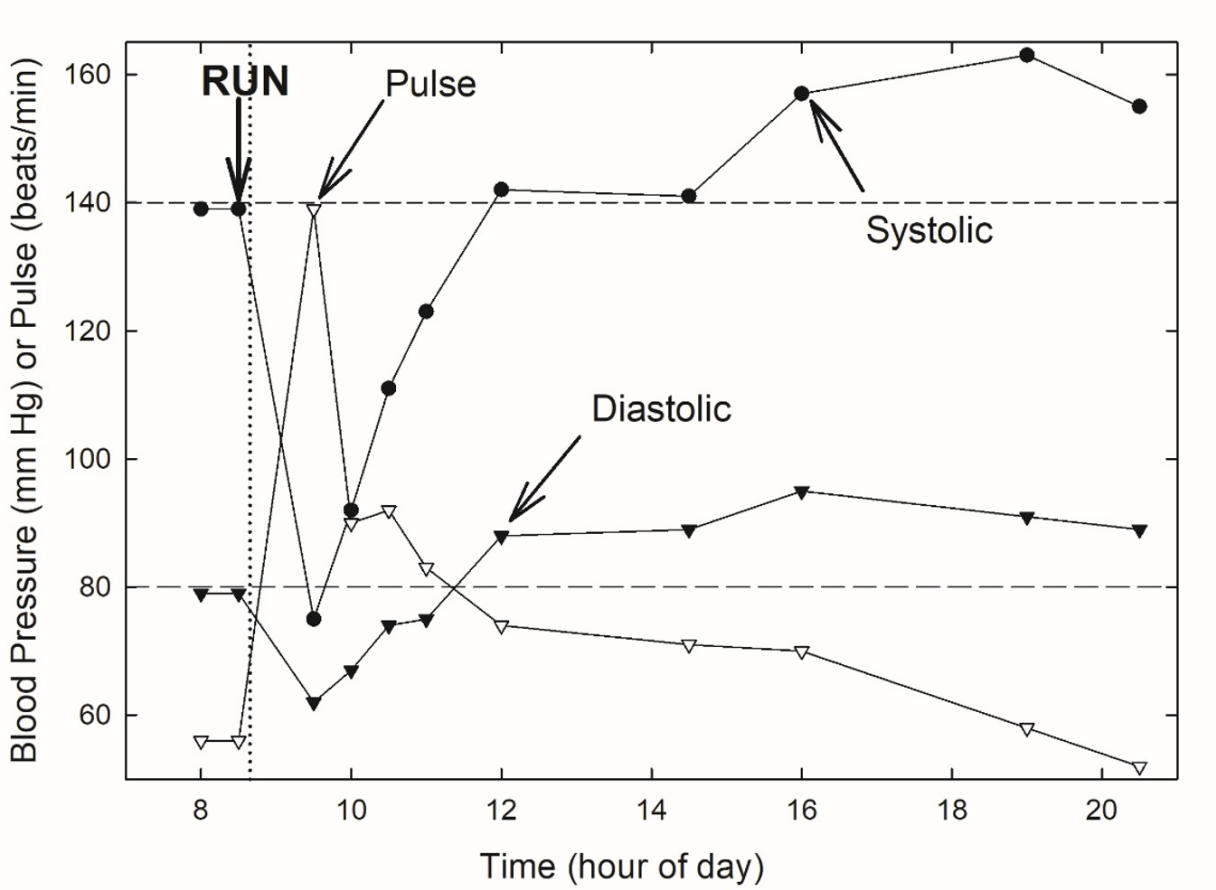

Figure 1. Changes in BP and pulse following a hypotensive episode while gently running seven days after a 5 th COVID-19 vaccination (second mRNA "booster"). Horizontal dashed lines indicate baseline values prior to running. The values corresponding to the start point ("RUN") are a repeat of those of 8-00 am, assuming minimal change in the interim (30 min). The vertical dotted line indicates the time of onset of tachycardia (approx. 10 min into the run). The long duration of the period from this to the first determination of BP and pulse values, should be noted. Pulse (open triangles); systolic BP (filled circles); diastolic BP (filled triangles).

My pulse was 140/min and systolic pressure was 75 mm Hg (Fig. 1). It took three hours of continued rest for my BP to return to normal and several more hours for my pulse to follow likewise. Given the new knowledge,[3][4][5] and having never in my 84 years experienced an episode like this, it is unlikely that it was unrelated to the vaccination. Following this episode (15th Oct 2022) I was well but discontinued jogging pending formal cardiac investigations and my own research, which is the main topic of this paper.

Formal investigations included echocardiograms and electrocardiographic monitoring during a treadmill "stress test" (21st January 2023) where speed increased slowly and my pulse achieved 130 beats/minute without undue breathlessness. Most blood tests were considered satisfactory, but atrial natriuretic peptide (NT-proBNP) was increased (182 ng/litre; normally <125 ng/litre). Nevertheless, my cardiologist advised that jogging could resume. Subsequent reexamination of my own BP records suggested caution in this respect.

Reexamination of blood pressure records

In the 1960s I was house physician to the hypertension research unit at a London teaching hospital. I subsequently explored other research avenues, but the diagnosis of mild hypertension in 2000 rekindled my interest, and my BP has been well-controlled with low ARB doses. Attempting to emulate normal baroreceptor-mediated controls, BP reading are recorded twice daily, and doses varied accordingly (see Methods). Given the above considerations, I retrospectively examined my records corresponding to the 2021-2023 period of COVID-19 vaccination.

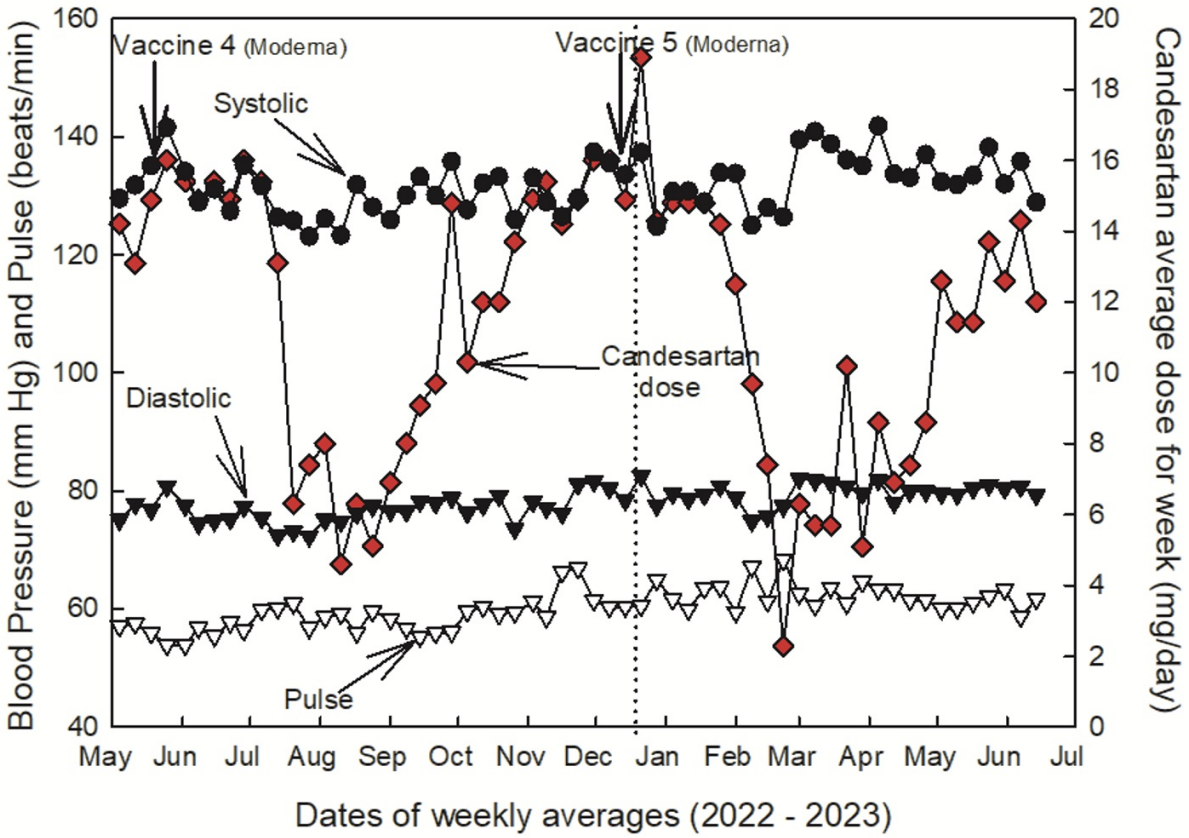

Figure 2. Influence of 4th and 5th COVID-19 mRNA vaccinations on BP, pulse, and required Candesartan dosages. Values of systolic BP (filled circles), diastolic BP (filled triangles), and pulse (open triangles), being kept relatively constant, the required dosage of Candesartan (red diamonds) acts as a *surrogate* indicator of what systolic blood pressure *might* have been. Vertical arrows indicate times of vaccinations. The vertical dotted line indicates the time of onset of tachycardia while running one week after the 5th vaccination (see Fig. 1). Individual data points indicating 7-day averages (ordinate), correspond to central Wednesdays with three days on either side (abscissa). The number of weeks between events can be approximated by counting the number of data points between them. Pulse values increased slightly (linear regression slope = 0·018; $r^{[2]}$ = 0·41; $P < 0·0001$).

Figure 2 refers to the 4th and 5th vaccinations. The hypotensive episode 7 days after the latter (Fig. 1), is noted by a vertical dotted line. As intended, systolic and diastolic BPs remained relatively constant around 130 and 75 (mm Hg), respectively. To maintain this constancy, Candisartan doses were modulated twice daily, decreasing when BP tended to rise, and increasing when BP tended to fall. Pulse values were also relatively constant, but linear regression showed a

significant slight increase.

Unexpectedly, seven weeks after the fourth vaccination (first booster), recorded BP values began to fall. The lower required candesartan dosages show that the fall would have been sustained for several weeks and then, should I have survived the episode, return to normal over the following ten weeks. During the latter part of this period, the fifth vaccination (second booster) was administered, but did not influence this recovery. However, thirteen weeks after this fifth vaccination, the required candesartan dosage showed an even greater decrease over a five-week period, followed again by a slow return to normal.

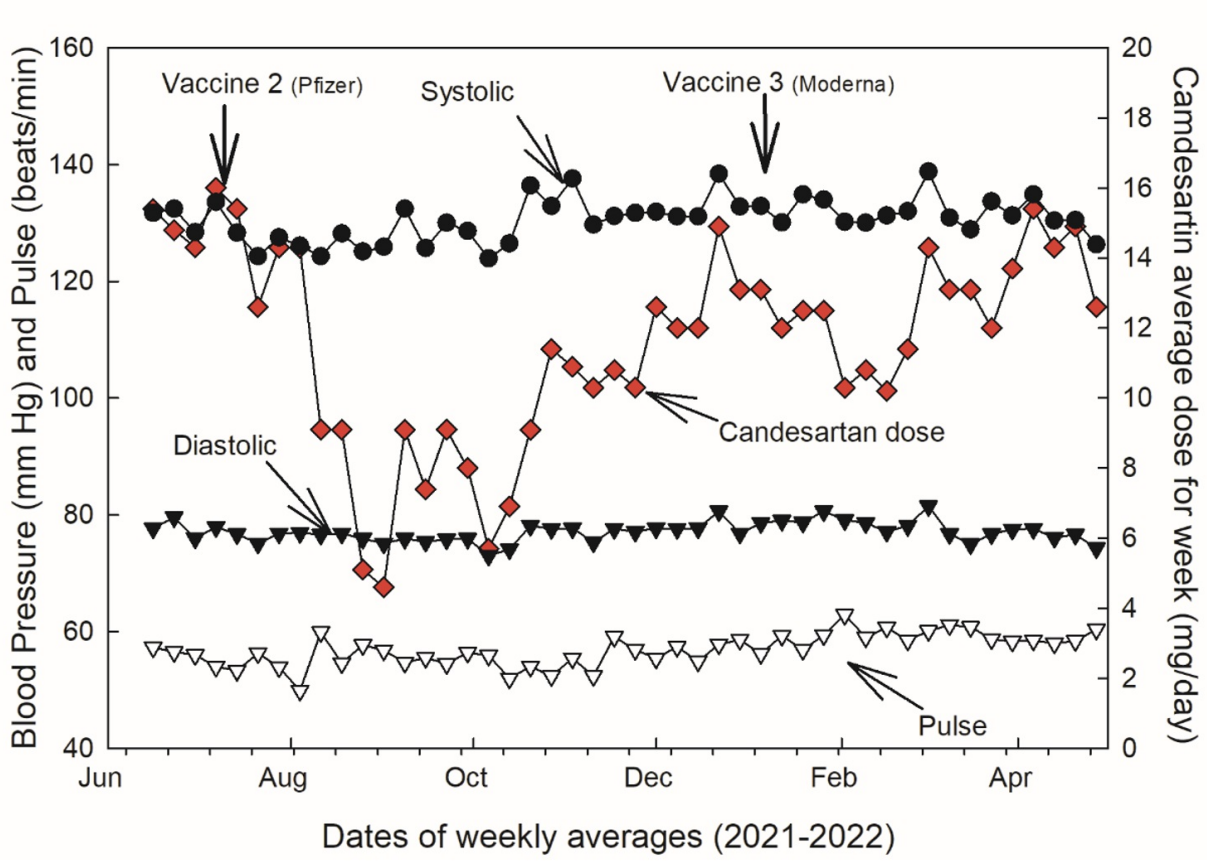

Figure 3. Influence of 2nd and 3rd COVID-19 mRNA vaccinations on BP, pulse, and required Candesartan dosage. Details are as in Fig. 2. Pulse values increased slightly (linear regression slope = 0·018; $r^{[2]}$ = 0·38; $P < 0·0001$).

These results were obtained with the Moderna mRNA vaccine. The second and third mRNA vaccinations included a different version (Table 1). Figure 3 shows that a less extreme fall in required dosage occurred four weeks after administration of the Pfizer version. This was sustained for ten weeks, followed by what appeared to be a recovery over ten weeks, which just preceded the third vaccination with a Moderna version. Surprisingly, the fall following this third vaccination occurred with little delay and was much smaller, being sustained for three weeks, followed by a recovery over seven weeks. As with Figure 2, the targeted values for systolic and diastolic BPs were sustained throughout this study period, but there was again a small progressive increase in pulse values.

Over these periods (Figs. 2, 3) Candesartan was the ARB of choice. However, at the time of the first vaccination, the

medication was Losartan, which had been employed since 2000. Here there was no clear evidence that the Pfizer vaccine had induced a dip a few weeks after injection. Overall, the temporal cause-and-effect relationship shown in figures 2-3 indicates increasing vulnerability to vaccine-induced hypotension over the study period, that was not dependent on the particular batch employed. A likely explanation for the hypotension is transient myocarditis.

Discussion

Despite an incomplete awareness of possible side-effects, the basic research of Katalin Karikó and others made mRNA-based vaccines available on time to save many lives in the COVID-19 pandemic.[18] Although the mRNAs were pretreated to increase their stability, no safe haven for them was expected. Thus, the mRNAs should soon degrade and any emerging side effects should be transient. The acceleration of research post-2020 was so rapid that preprint postings became the norm for many of us working in the field.

Underreporting, especially in the elderly

Following the first report of Watanabe and Hana on the post-vaccination mortality risk of myocarditis becoming increasingly evident (October 18th, 2022), there was a lively debate in the comments column of the *medXriv* preprint server, accompanied by many tweets (>10,000; unusual for that server). Their conclusions were repeated in a subsequent posting (December 22nd 2022): [3]

> *SARS-CoV-2 vaccination was associated with higher risk of myocarditis death, not only in young adults but also in all age groups including the elderly. Considering healthy vaccinee effect, the risk may be 4 times or higher than the apparent risk of myocarditis death. Underreporting should also be considered. Based on this study, risk of myocarditis following SARS-CoV-2 vaccination may be more serious than that reported previously.*

With increasing recognition of shortcomings of earlier studies,[11] there is now a growing consensus in the field regarding this conclusion.[12][13][19] An important recent advance is the detection of vaccination-induced circulating viral spike protein in 16 young non-cryptic myocarditis cases, but not in 45 age-matched asymptomatic vaccinated controls.[20]

Implications of the present study

The term “cryptic evidence” in the title of this paper implies a novel approach to myocarditis assay (otherwise the evidence would have remained cryptic). Thus, the paper describes the careful application of a standard BP monitor and analysis of its readings in relationship to times of vaccination. To my knowledge, the close, and repeated, linkage of successive COVID-19 vaccinations to falls in BP implies a cause-and-effect relationship that has not previously been reported.

Although a case report, the present identification of cryptic factors likely to have contributed to the author’s myocarditis further supports Watanabe and Hana.[3] Special support came from his retrospective monitoring of BP responses to ARBs

over past decades,[6] that included the period of the pandemic.Although confined to this class of antihypertensive agent, it is likely that the results will be found to apply to other classes. However, ARBs have played a more complex role in the pandemic as outlined in the Introduction to this paper, so caution must be exercised.

From the present study, a distinction can be drawn between short-term post-vaccination side effects occurring in the days immediately after vaccination and those occurring much later. The first, most common, category would include systemic and/or localized inflammatory responses (Table 1) which, in the case of a heart under stress, might trigger arrythmia and acute functional impairment (Fig. 1). However, localized off-target responses could initiate tissue damage, culminating, sometimes after many weeks, in measurable functional impairment (Figs. 2,3). Whether short or long term, when cryptic (e.g., as when not provoked by exercise), these myocarditis side-effects could be the source of unexplained deaths among vaccinated persons, some of whom may have had preexisting cardiac problems. Indeed, early in the pandemic there was a report of transient cardiac symptoms in an elderly male *three months* after his second dose of mRNA vaccine. Here there were preexisting morbidities (narrow coronary artery and hypertension).[21] A similar post-vaccine late-onset symptomology was recently reported for *three* cases treated with immune checkpoint inhibitors, which would have decreased normal constraints on T-cell mediated autoimmunity.[22]

Regarding mechanism, when heart failure is due to elevated peripheral vasoconstriction an appropriate remedy is to decrease the vasoconstriction with conventional antihypertensive medications. In this circumstance, there is usually a *reciprocal* relationship between systolic BP and pulse. As the BP increases the pulse decreases, and vice-versa. However, hearts can fail for central cardiac reasons. When this is the primary cause, baroreceptor reflexes may promote heart rate (pulse). In this circumstance, BP and pulse may be coordinately *increased*. Antihypertensive treatment could then lead to an uncompensatable degree of hypotension. A similar problem has been identified previously in relation to a peripheral cause, namely the relaxation of vasculature in response to high environmental temperatures, which seemed to be explicable based on differential signaling by countervailing receptors.[6] As is now increasingly recognized, this circumstance dictates decreasing antihypertensive dosage below that employed with normal temperatures.[15] A recent review by Maeda et al. provides insightful discussion of the possible underlying physiology.[23] While cautioning against strenuous activity, Altman et al.[24] note that “the long-term effects of even mild vaccine-associated myocardial injury are unknown, and resolved cases may exhibit some degree of permanent damage such as interstitial fibrosis.”

While vaccination against coronavirus infection has, and will continue, to save the lives of millions, in the long-term, investigations of specific vulnerabilities, both of viruses and of their hosts, are warranted. Viral vulnerabilities should be clarified to focus chemotherapeutic agents to specific viral target regions,[25] and the ancestral histories of different host groups should work to guide choices among those agents.[7] On the fourth of August 2023 the author resumed his biweekly jogging.

Conclusions

Evidence before this study

After general safety tests, COVID-19 mRNA vaccines were given emergency approval. Reports of side-effects, some extending beyond the “rare” category, have since emerged. The present work builds on the author’s previous study of the potential danger of not lowering dosage of antihypertension medication in hot climates.

Added value of this study

An unsuspected relationship between mRNA vaccination and hypotension several weeks later is revealed.

Implications of the available evidence

Post-vaccination deaths of those on antihypertensive medication might have been avoided. The simple methodology might facilitate “crowd source” confirmation and hence consideration of cryptic factors in statistical analyses. If a vulnerable population subset is identified, the genetic and/or environmental factors that correlate with that vulnerability might be identified. The “time in therapeutic range” (TTR) approach to BP medication might be more widely appreciated.

Statements and Declarations

Data availability statement

The figures support the conclusions of this article. The raw data will be made available by the author, without undue reservation.

Ethics statement

The author took readings of his own blood pressure. No institutional ethics board approval is required for “self-experimentation” (rule 5 of 1949 Nuremberg Code).

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Conflict of interest

The author declares no competing interests.

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Machine internet archive host the author's webpages.

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Added note

This preprint paper was prepared in December 2023. Further developments are described in a peer-reviewed paper that was accepted for publication on June 14th 2024.[26]

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