Editorial

Vaccination Against Heart Attack?

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Abstract: A detailed look into the published record reveals that some of the arguments were derived from generalizations of observed results across different studies. The lynchpin of such attempts lies in an understanding of underlying phenomena in order to provide a reasoned justification for such sweeping generalities. Here, we highlight selected areas where the published record does not speak with one voice and where future work is needed to explicate apparently diverging lines of observation.

Keywords: Clinical Case Report, Immunological Context, Generalization

In the United States, it is estimated that heart attacks strike one individual every 43 sec (Mozaffarian *et al.*, 2016). Correspondingly, 24% of the recorded deaths in the United States in 2012 were caused by heart disease (Siegel *et al.*, 2016). An analysis of the death certificates for the year 2013 revealed that heart failure was indicated in 1 out of 9 cases (Mozaffarian *et al.*, 2016). All these numbers make one wonder how useful it would be if vaccination could provide protection against heart attacks.

To answer this question, or to provide argument in favor of a systematic clinical trial, one is forced to consult the published record.

In an editorial, Søgaard (2015) alerts readers to the caveat, as pointed out by Ren *et al.* (2015) as well, that the pneumococcal polysaccharide vaccination was, in some cases, administered to patients with a higher risk of acute coronary syndrome and/or stroke, which would introduce a bias. Furthermore, Søgaard (2015) points out that two studies, namely (Lamontagne *et al.*, 2008; Eurich *et al.*, 2012), report an unusually striking effect of pneumococcal polysaccharide vaccination on acute coronary syndrome when compared to the other studies, evaluated by (Ren *et al.*, 2015).

There is precedent for the use of attenuated or subunit vaccines in the clinical management of infectious diseases. Refer to Borba *et al.* (2015; Salk and Salk,

1977; Pulendran and Ahmed, 2011) as guide for further reading. This approach hinges on the ability of antibodies to recognize the infectious antigen and mark them for destruction. Logically, one may now ask whether myocardial infarction is an infectious disease in fulfillment of the Henle-Koch postulates (Evans, 1976). There appears to be no indication to the knowledge of the authors that would provide reasonable evidence in support of an answer in the affirmative.

In the apparent absence of direct evidence, one is then forced to consider indirect evidence for either myocardial infarction being an infectious disease in the classical sense or whether there is precedent in the literature that would provide justification above and beyond a reasonable doubt for patient's benefits derived from either an appropriate vaccination event or antibodies generated as a result of an infection. As a result, the lingering argument of whether a true comparison of study population is justified needs careful consideration; we have made similar lines of reasoning available elsewhere and shall incorporate them as stated in appropriate context by reference of (Schmidt and Brown, 2015a; 2015b).

At first glance, there appears to be a serological correlation with higher class γ and α antibodies of patients as measured by ELISA and tabulated as highest dilution where an optical density of 0.3 was

observed (Saikku *et al.*, 1988). The authors reported dilutions of $\geq$ 128 for class γ and $\geq$ 32 for class α antibodies against the Taiwan acute respiratory agent strain of *Chlamydia pneumonia* (referred to as type strain TW-183 and isolated in 1965 from a child in Taiwan; Grayston *et al.*, 1989; Kuo *et al.*, 1995) with a p = 0.00001 for acute myocardial infarction group versus control and p = 0.003 for chronic coronary heart disease versus control. The authors could not find a significant correlation (defined as p>0.05) when the chronic coronary heart disease group was compared with the acute myocardial infarction group (Saikku *et al.*, 1988). Additional support for this notion is provided by a completely independent study where the *C. pneumonia* strain IOL 207 was used to test patient's sera to argue that further effort is needed to shed light onto the pathogenesis of coronary heart pathologies (Mendall *et al.*, 1995).

The above-mentioned evidence points to the involvement of two strains of *C. pneumonia* in pathologies involving coronary heart disease, whilst one strain (TW-182) is implicated to be involved in myocardial infarction, whereas another one, IOL-207, albeit indirectly by virtue of using it as a target to test patients' sera, is ascribed to be of concern in the pathologies of coronary heart disease. *If so* and *how* and *when* and *how often*, to name a few of the questions that come to mind, remain to be worked out individually and collectively using the whole spectrum of technology available to us; Storsberg and Schmidt (2015) as an introduction.

What about the more than 20 isolates referred to in Grayston *et al.* (1989)? Are all of them identical with regard to their immunological features? Doubt on this notion was cast by Wagels *et al.* (1994), where patient's antibodies recognize a pattern of bands in a Western blot of different isolates (Wagels *et al.*, 1994).

Looking from the other side, namely published data pertaining to myocardial infarction and antibodies, one study, for instance, provides data showing that patients at risk of suffering from acute myocardial infarction, at time of analysis, exhibit an elevated level of class γ anti-oxidized low-density lipoprotein while after 30 days of follow-up, the levels of these γ decreased while the levels of μ antioxidized low-density lipoprotein increased (all statistically significant with p values below 0.01; Tsimikas *et al.*, 2003). Whilst there is no doubt that the observation is significant, the immunological concept of *baseline* or alternatively expressed as *natural class γ antibodies* is not easily defined because memory B cells could secrete γ and, equally, B cell clones could secrete γ in response to contact with foreign material, such as invading pathogens (Gronwall and Silverman, 2014).

The above provides a convincing impetus for a serological monitoring of a given study group to ensure qualified comparisons between study groups are employed if one sets out to argue, say, that there is 'no evidence of association between Chlamydia pneumoniae IgG seropositivity and risks of future myocardial infarction' (quote taken from Ridker *et al.*, 1999; supportive statements are provided by an independent study, e.g., Nieto *et al.*, 1999).

Conclusion

Serological information accompanying study reports are needed to avoid a comparison of potentially incompatible study groups. Qu *et al.* (2013) as an example of highlighted issues surrounding an accurate and precise detection of infectious particles in a group of patients.

Acknowledgement

Author's Contributions

Joachim Storsberg and Mark A. Brown: Provided critical input and assisted in revising and improving the paper.

Christian Schmidt: Wrote the first draft of the paper and provided critical input and assisted in revising and improving the paper.

Ethics

Joachim Storsberg, Christian Schmidt and Mark A. Brown report no conflicts of interest with regard to this report. Mark A. Brown and Christian Schmidt are members of the Editorial Board of The American Journal of Immunology, are waived from the Article Processing fee for this contribution and receive no remuneration for the editorial work, either individually or collectively.

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