

Covid-19 Vaccine: is it a Deed of Daring for the Heart in the House of ADE?

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ABSTRACT

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) represents an ongoing global challenge and it is placing considerable strain on healthcare and economic systems. Covid-19 often presents as an acute cardiac injury cardiomyopathy, in the absence of obstructive coronary artery disease denominated ACovCS. Research has called attention to several mechanisms related to cardiovascular involvement and lately, growing evidences link heart dysfunction to an intricate cross talk between Toll-Like Receptor and Notch signaling pathways. Up to date, no proven effective therapies currently exist and worldwide there is a great expectancy of a vaccine. In this context perplexing

concern regards possible antibody dependent enhancement (ADE) of SARS-CoV-2 and the potential role of Th17 responses on eosinophilic immunopathology. Until now, Covid-19 vaccine would seem a deed of daring for the heart in the house of ADE. The hope is that a safe and protective vaccine could represent the most effective strategy also for prevention of future outbreaks of this virus and that in addition it might open new paths on the cardioprotective effects of vaccination.

Key words: ADE; Covid-19; SARS-CoV-2; *Th17*; vaccine

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TEXT

'διογενὲς Λαερτιάδη, πολυμήχαν' Ὀδυσσεῦ,
σχέτλιε, τίπτ' ἔτι μείζον ἐνὶ φρεσὶ μήσεαι ἔργον;
πὼς ἔτλης Ἄϊδόσδε κατελθέμεν, ἔνθα τε νεκροὶ
ἀφραδέες ναίουσι, βροτῶν εἶδωλα καμόντων.'

'Ulysses, noble son of Laertes, what deed of daring will you undertake next, that you venture down to the house of Hades among us silly dead, who are but the ghosts of them that can labour no more?' *Odyssey XI, 473-476*^[1]

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) represents an ongoing global challenge and it is placing considerable strain on healthcare^[2] and economic systems. In addition to the airway and lung involvement signs, Covid-19 can manifest with a variety of clinical presentations, but often presents as an acute cardiac injury cardiomyopathy, with ventricular arrhythmias and hemodynamic instability^[3,4,5] in the absence of obstructive coronary artery disease denominated Acute COVID-19 Cardiovascular Syndrome (ACovCS)^[6]. Increasing evidence suggests that an aggressive treatment may be considered for patients with underlying cardiovascular disease (CVD) because their ACovCS high risk and that their prognosis in absence

of ACovCS is relatively favorable^[4] while severe morbidity and fatal outcome may have far more to do with ACovCS than pulmonary failure^[7]. Research has called attention to several mechanisms related to cardiovascular involvement such to acute coronary syndrome, demand ischemia, microvascular injury, cytokine-mediated injury, myocarditis or stress-related cardiomyopathy^[3,6,7] as well research has proposed a surveillance, diagnostic and management strategy balancing potential patient risks and healthcare staff exposure leading to improvement in meaningful clinical outcomes^[3,6]. Lately, growing evidences have pointed cardiovascular research interest to host Th17 inflammatory responses linking heart dysfunction to IL-17 producing T cells and IL-17-promoting cytokines^[7] and involving an intricate cross talk between Toll-Like Receptor TLR and Notch signaling pathways^[8,9]. Of great interest, research has been demonstrated that proatherogenic factors promote the polarization and inflammatory function of autoimmune Th17 cells, which may be critical for the pathogenesis of atherosclerosis and other related autoimmune diseases^[10]. Up to date, no proven effective therapies currently exist^[3] and worldwide there is a great expectancy of a vaccine. In this context perplexing concern regards possible antibody dependent enhancement (ADE) of SARS-CoV-2 and the potential role of Th17 responses^[7] on eosinophilic immunopathology (EI) development^[8] that potentially could have several implications in terms of the production and clinical development of COVID-19 vaccines. The mechanisms of possible immune enhancement from coronavirus vaccinations are still not well understood and conflicting opinions exist. In some cases, EI has been postulated as a component of ADE while others research differentiate EI from ADE^[7], and there may also be the hypothesys of a partial overlap^[8]. Until now, clinical data has not fully established an ADE role in human COVID-19^[11] and some experts doubt that ADE could be relevant in this disease^[7,11]. A great debate is growing on potential pitfalls and strategies toward an effective vaccine^[7,11] though, up to date, given the premises, it would seem a deed of daring for the heart in the house of ADE^[1]. The hope is that a safe and protective vaccine could represent the most effective^[12] strategy also for prevention of future outbreaks of this virus and that in addition it might open new paths on the cardioprotective effects of vaccination^[13].

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