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Reply to Flamaing's Letter

I was pleased to read the comments of Flamaing about the need for a more ample vaccination approach, to better protect the elderly population through influenza vaccination in various population groups.

Enhancing vaccination rates in one of the largest portions of the contagious population, i.e., children, is certainly a good idea and, as reported by Flamaing, there is some evidence that influenza vaccine efficiency reduces flu in this population (1). However, one cannot skip the gap and, to my knowledge, there is only one study demonstrating the efficiency of flu vaccination of children reducing flu incidence, death rates and medical consumption among elderly population (2). The article cited by Flamaing concerns only the efficiency of flu vaccination in decreasing flu incidence in household adults and not in the elderly population (2). In addition, there is no consensus ascertaining that decreased flu rates in children will decrease flu rates in the whole population (1). In addition, the main difference between Flamaing's proposal and the theoretical benefits I proposed in the manuscript is that, although there are only a few of them, at least several studies have demonstrated the benefits of HCW flu vaccination in reducing influenza-related death in elderly persons living in nursing homes (3).

Also, it is a postulation to say that the decision of the Committee on Immunization Practices in the US recommending routine vaccination of children against influenza is based on the effect of potential herd immunity in community-dwelling populations. This may also first protect a special group (children) who are indirectly responsible for the absence of working adults.

Lastly, if a broader strategy is needed to enhance vaccine coverage in different target populations, we must be careful to determine them appropriately, so that we are not put in the position, later, of having to cope with misunderstood messages by the general population.

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Reply to Flamaing's Letter

Dr. Flamaing's comments on the various papers published in *Aging Clinical and Experimental Research* on Vaccines in Ageing European citizens (1-3) were very welcome, because they stressed important and interesting points.

The need for "life course vaccine guidelines" was stressed by Flamaing, who insisted on herd immunity, and we have absolutely no doubt about its importance. To our knowledge, this was the first time that the idea of "life course vaccine guidelines" has been proposed by geriatricians in the special issue of the journal. Geriatricians can raise the concept, but they cannot lay down vaccination rules for children, even if it has been demonstrated in Japan that influenza vaccination of children can decrease global excess deaths from pneumonia and influenza (4).

As stated clearly in the paper by Michel et al., geriatricians and vaccine experts know that the immune response to current vaccines is not optimal, considering the problem of immunosenescence. However, the proposal of vaccine guidelines for the immunosenescent population will protect more individuals than in the past, while awaiting the production of new vaccines, more suitable for this frail and often malnourished old population (5).

The debate concerning the use of pneumococcal polysaccharide 23-valent vaccine (PPSV23) is an old one but it is currently the only pneumococcal vaccine available for adults. The debate is stimulated by the first trials of the not yet labelled 13-conjugated pneumococcal vaccine for adults (6, 7). There is no doubt that the PPSV23 vaccine is useful in adults and at-risk populations: Merck & Co. calculated the numbers needed to vaccinate based on a variety of populations: a) for the over-65's, the number needed to prevent an Invasive Pneumococcal Disease (IPD) case with a 10-year duration of protection was about 1200; b) when patients with co-morbidities aged 18-64 are added, the number falls to 662 (8). Recent studies in older adults have examined the immunological responses among persons given either a polysaccharide vaccine or conjugate vaccine, followed by another dose of polysaccharide or another dose of conjugate: a) the vaccine has a limited duration of protection (estimated at around 8 years); the person's risk increases with age; b) Dr. Flamaing was right when arguing that the CDC recommended 1 dose of PPSV23 for most people in a lifetime and 2 doses for certain people. However, c) the overall generalization from recent studies is that it appears that, if a polysaccharide vaccine is given before the conjugate vaccine, the response to the conjugate is lower than with primary vaccination; whereas, if the conjugate vaccine is given first, there does not seem to be a decreased response with a subsequent dose of either vaccine (7).

Another important point to be considered is that influenza infection predisposes individuals to secondary bacterial pneumonia (9). With the knowledge that, during the pre-antibiotic flu pandemics, IVP explained at least 20% of deaths (10), the need to propose PPSV23 during the pre-pandemic phase was debated in depth. Until now no formal answer was given on the economic burden of the vaccine use. In any case this evaluation would take into account the probable decrease of antibiotic prescription and as a consequence the decrease of antibiotic resistance (11).

For all the above-mentioned arguments, I do not think there is any need to modify the vaccination recommendations of the EUGMS-IAGG-ER.

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