Proteins that contaminate influenza vaccines have high homology to SARS-CoV-2 proteins thus increasing risk of severe COVID-19 disease and mortality

Vinu Arumugham

Aug 2020

vinucubeacc@gmail.com

Abstract

Influenza vaccines are manufactured using chicken eggs, canine kidney cells or insect cells. Chicken and dogs can be infected with numerous viruses including coronaviruses. Therefore influenza vaccines can be contaminated with coronavirus proteins. These coronavirus proteins of course have high homology to SARS-CoV-2 proteins. Further, we show that even chicken egg proteins have high homology to SARS-CoV-2 proteins. Influenza vaccine administration is known to create IgE mediated sensitization (allergy) to all proteins in the vaccine. In fact, vaccine-induced egg allergy is required for the vaccine to work and protect against influenza. This is because most influenza vaccines lack an adjuvant and they depend on the allergic reaction at the injection site to provide an adjuvant effect.

Upon COVID-19 infection, patients will suffer an allergic reaction due to cross reaction against SARS-CoV-2 proteins. This predictably produces anaphylaxis symptoms. Since the viral load increases over a few days, we have slow rolling anaphylaxis. The result is damage to multiple organs. Acute respiratory distress syndrome results from lung damage. Cardiac injury due to Kounis syndrome. Coagulation dysfunction, hypotension and shock are other possible outcomes. As in anaphylaxis treatment, epinephrine, histamine H1 and H2 blockers, etc. help prevent or treat these conditions.

Introduction

Most influenza vaccines are manufactured using specific pathogen free (SPF) chicken eggs. The SPF specification covers 18 pathogens but that list (1) does not include coronaviruses. So chicken and the SPF eggs they produce can be infected with coronaviruses. Madin-Darby Canine Kidney (MDCK) cells are also used to manufacture some influenza vaccines (2).

MDCK cells are susceptible to coronavirus infections (3). So MDCK cells derived from infected dogs can be contaminated with coronavirus proteins. Contamination of vaccines with viruses from infected animal tissues used in vaccine manufacturing, is not uncommon. The rotavirus vaccine contains viable porcine circoviruses, for example (4,5).

Influenza vaccine protection depends on vaccine-induced egg allergy

Influenza vaccines create long term persistent IgE mediated sensitization (allergy) to all proteins in the vaccine, including the influenza viral proteins (6–10). Upon subsequent influenza infection, people can suffer an allergic reaction to the influenza virus itself, which similar to COVID-19, can lead to a cytokine storm and influenza shock syndrome (11).

Jacob et al. (12). identified 293 chicken proteins in the influenza vaccine. Injecting such chicken egg proteins into humans induces long term persistent IgE mediated sensitization to these proteins (10). Subsequently administered egg protein-containing influenza vaccines elicit an allergic reaction at the injection site. This reaction provides the innate immune system costimulation required (adjuvant effect) to produce the protective immune response against influenza proteins in the vaccine. This is the reason why when the influenza vaccine is administered for the very first time, it does **not** produce an effective protective response. The CDC recommends a second dose of the vaccine to address this issue when a child receives an influenza vaccine for the first time (13). In other words, the influenza vaccine depends on sickening people with egg allergy, to produce its protective effect.

The Flublok influenza vaccine is egg-free (14). So as expected, it would elicit only a weak protective response. The solution? They increased the antigen content to 300% compared to a regular egg derived influenza vaccine. So the Flublok vaccine contains 45 mcg of each hemagglutinin (HA) protein compared to 15 mcg in the regular vaccine.

Vaccine-induced allergy causes COVID-19 severity

Therefore, as above, coronavirus proteins that contaminate the influenza vaccine as well as chicken proteins that have similarity to SARS-CoV-2 proteins, cause allergic sensitization to all those proteins. Upon subsequent COVID-19 infection, due to the cross reaction, people will suffer a severe allergic reaction which explains COVID-19 severity in a section of the population. Detailed BLASTP protein sequence analysis results showing homology between chicken and SARS-CoV-2 proteins are provided in a later section. Nursing home residents are likely to have higher influenza vaccine coverage. So predictably, they have a very high risk of suffering severe COVID-19.

This is the reason why allergy medications such as antihistamines (cetirizine, famotidine) and mast cell stabilizers help in COVID-19 (15–17). In general, since COVID-19 is simply a slow rolling version of anaphylaxis, proven anaphylaxis treatments will work (18).

Cardiac injury that occurs due to an allergic reaction is known as Kounis syndrome. The same injury occurs in influenza shock syndrome, COVID-19 and dengue because they all involve an allergic reaction. The details were previously described (19).

Conclusion

Contaminated vaccines, including influenza vaccines, contribute to COVID-19 severity and mortality. While this article focused on influenza vaccines, all vaccines have a similar problem (5). COVID-19 severity is the latest to be added to the huge list of diseases caused by contaminated vaccines (20).

Epidemiological studies are unreliable. One study will claim influenza vaccine is associated with COVID-19 severity and another one will claim it is not associated. The Institute of Medicine (IOM) now known as the National Academy of Medicine (NAM) found that vaccine safety epidemiological studies are useless, 93% of the time (21). We present reliable, mechanistic evidence of causation.

Detailed BLASTP result examples

QHD43415.1 orf1ab polyprotein [Severe acute respiratory syndrome coronavirus 2] vs.

XP_025008461.1 poly [ADP-ribose] polymerase 14 isoform X3 [Gallus gallus]

Alignment statistics for match #1

Score	Expect	Method	Identities	Positives	Gaps
60.1 bits(144)	1e-07	Compositional matrix adjust.	57/183(31%)	86/183(46%)	22/183(12%)

```
Query  1056  VVVNAANVYLKHGGGVAGALNKATNNAMQVESDDYIATNGPLKVGGSCVLSGHNLA-KHC  1114
             VVVNA+N  LKH GG+A AL +A    +Q E D  +  +G L+ G + +     L  K
Sbjct  864   VVVNASNEDLKHIGGLAWALLQAAGPELQAECDGVVRMSGSLQAGDAVITGAGKLPCKQV  923

Query  1115  LHVVGPNVNKGED---IQLLKSAY-------ENFNQHEVLLAPLLSAGIFGADPIHSLRV  1164
             +H VGP   + +    + LLK          E +N H  +  P +S GIFG  P+H
Sbjct  924   IHAVGPRWKEQDAEKCVYLLKKTIKKSLQLAETYN-HRSIAFPSVSGGIFGF-PLHK---  978

Query  1165  CVDTVRTNVYLAVFDKNLYDKLVSSFLEMKSEKQVEQKIAEIPKEEV-KPFITESKPSVE  1223
             CV     N  ++   K L +    S L+      V+++   + +E V K F  +S  SV
Sbjct  979   CV-----NAIVSAIKKTLEEFKRDSSLKEIHLVAVDEETVRVLRETVQKEFTAKSSSSVL  1033

Query  1224  QRK  1226
             Q++
Sbjct  1034  QQQ  1036
```

QHD43415.1 orf1ab polyprotein [Severe acute respiratory syndrome coronavirus 2] vs.
XP_015131826.1 protein ZGRF1 [Gallus gallus]

Alignment statistics for match #1

Score	Expect	Method	Identities	Positives	Gaps
55.5 bits(132)	3e-06	Compositional matrix adjust.	68/258(26%)	112/258(43%)	52/258(20%)

```
Query  5694  IVVFDEISMATNYDLSVVNARLRAKHYVYIGDPAQLP----APRTLLTKGTLEPEYFNSV  5749
             +VV DE S  T     +  AR + +  V +GDP QLP       ++  KG LE   F+ +
Sbjct  1488  VVVLDECSQMTEPTSLLPIARFQCEKLVLVGDPKQLPPTIQGSESIHEKG-LEQTLFDRL  1546

Query  5750  CRL-MKTIGPDMFLGTCRRCPAEIVDTVSALVYDNKL---KAHKDKS-------AQCF--  5796
             C +  KTI     L T  RC    I    + L Y+  L    + K++S         CF
Sbjct  1547  CLMGHKTI----LLRTQYRCHPAISAIANELFYEGNLIDGVSEKERSPLLDWLPTLCFYS  1602

Query  5797  ----------KMFYKGVITH--------DVSSAINRPQIGVVREFLTRNPAWRKAVFISP  5838
                        FY     H         ++S I+   +GV+  +  ++  ++    +
Sbjct  1603  VNGLEQIERDNSFYNMAEVHFTVKFIQALIASGIDGSAVGVITFY--KSQMYKLQNLLRS  1660

Query  5839  YNSQNAVASKILGLPTQTVDSSQGSEYDYVIFT--QTTETAHSCNVNRFNVAITRAK---  5893
              +S+   A  +  +   TVD+ QG+E + V+ +  +T +T  + +  R NVA+TRAK
Sbjct  1661  IHSE---AFPVKAVQVSTVDAFQGAEKEIVVLSCVRTRQTGFTDSEKRMNVALTRAKRHL  1717

Query  5894  --VGILCIMSDRDLYDKL  5909
               VG L  +S   LY+++
Sbjct  1718  LIVGNLACLSKNRLYERV  1735
```

References

1. EUROPEAN PHARMACOPOEIA 7.0 5.2.2. EUROPEAN PHARMACOPOEIA 7.0 5.2.2. SPF chicken flocks for vaccines 5.2. GENERAL TEXTS ON BIOLOGICAL PRODUCTS 5.2.1. TERMINOLOGY USED IN MONOGRAPHS ON BIOLOGICAL PRODUCTS [Internet]. [cited 2020 Aug 21]. Available from: https://www.valobiomedia.com/content/ep7.0_5.2.2_spf_flocks.pdf
2. Flucelvax Quadrivalent | FDA [Internet]. [cited 2019 Sep 9]. Available from: https://www.fda.gov/vaccines-blood-biologics/vaccines/flucelvax-quadrivalent
3. Chen YN, Hsu HC, Wang SW, Lien HC, Lu HT, Peng SK. Entry of scotophilus bat coronavirus-512 and severe acute respiratory syndrome coronavirus in human and multiple animal cells. Pathogens [Internet]. 2019 Dec 1 [cited 2020 Aug 22];8(4). Available from: /pmc/articles/PMC6963420/?report=abstract
4. CDC, Ncird. Centers for Disease Control and Prevention Epidemiology and Prevention of Vaccine-Preventable Diseases,13th Edition [Internet]. [cited 2020 Jan 17]. Available from: https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/appdx-full-b.pdf
5. Arumugham V. Immunological mechanisms explaining the role of IgE, mast cells, histamine, elevating ferritin, IL-6, D-dimer, VEGF levels in COVID-19 and dengue, potential treatments such as mast cell stabilizers, antihistamines, Vitamin C, hydroxychloroquine, ivermecti [Internet]. 2020 [cited 2020 Apr 24]. Available from: https://doi.org/10.5281/zenodo.3748303
6. Smith-Norowitz TA, Wong D, Kusonruksa M, Norowitz KB, Joks R, Durkin HG, et al. Long term persistence of IgE anti-influenza virus antibodies in pediatric and adult serum post vaccination with influenza virus vaccine. Int J Med Sci [Internet]. 2011 Mar 18 [cited 2019 Jan 11];8(3):239–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21448311
7. Davidsson A, Eriksson JC, Rudblad S, Brokstad KA. Influenza Specific Serum IgE is Present in Non-Allergic Subjects. Scand J Immunol [Internet]. 2005 Dec [cited 2019 Jan 11];62(6):560–1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16316424
8. Nagao M, Fujisawa T, Ihara T, Kino Y. Highly increased levels of IgE antibodies to vaccine components in children with influenza vaccine-associated anaphylaxis. J Allergy Clin Immunol. 2016 Mar;137(3):861–7.
9. Nakayama T, Kumagai T, Nishimura N, Ozaki T, Okafuji T, Suzuki E, et al. Seasonal split influenza vaccine induced IgE sensitization against influenza vaccine. Vaccine [Internet]. 2015 Nov 9 [cited 2019 Jan 11];33(45):6099–105. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26188254
10. Yamane N, Uemura H. Serological examination of IgE- and IgG-specific antibodies to egg protein during influenza virus immunization. Epidemiol Infect [Internet]. 1988 Apr;100(2):291–9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/3356225
11. Arumugham V. Influenza vaccines and dengue-like disease [Internet]. The BMJ. 2018. Available from: https://www.bmj.com/content/360/bmj.k1378/rr-15
12. Jacob L, Leib R, Ollila HM, Bonvalet M, Adams CM, Mignot E. Comparison of Pandemrix and Arepanrix, two pH1N1 AS03-adjuvanted vaccines differentially associated with narcolepsy development.

Brain Behav Immun [Internet]. 2015 Jul [cited 2019 Nov 2];47:44–57. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25452148

13. Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices—United States, 2018–19 Influenza Season. MMWR Recomm Reports [Internet]. 2018 Aug 24 [cited 2019 Apr 15];67(03):1–20. Available from: http://www.cdc.gov/mmwr/volumes/67/rr/rr6703a1.htm?s_cid=rr6703a1_w

14. Corporation PS. Flublok Quadrivalent 2017-2018 [Internet]. 2018. Available from: https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM524684.pdf

15. Malone R et al. COVID-19: Famotidine, Histamine, Mast Cells, and Mechanisms [Internet]. Preprint. 2020 [cited 2020 Jul 7]. Available from: https://doi.org/10.21203/rs.3.rs-30934/v2

16. Hogan RB, Hogan RB, Cannon T, Rappi M, Studdard J, Paul D, et al. Dual-Histamine Blockade with Cetirizine - Famotidine Reduces Pulmonary Symptoms in COVID-19 Patients. medRxiv [Internet]. 2020 Jul 6 [cited 2020 Jul 7];2020.06.30.20137752. Available from: https://doi.org/10.1101/2020.06.30.20137752

17. Tomera K, Kittah J. FAMOTIDINE WITH CELECOXIB ADJUVANT THERAPY ON HOSPITALIZED COVID-19 PATIENTS: A CASE SERIES [Internet]. 2020 [cited 2020 Jul 8]. Available from: https://papers.ssrn.com/abstract=3646583

18. Lieberman P, Kemp SF, Oppenheimer J, Lang DM, Bernstein IL, Nicklas RA, et al. The diagnosis and management of anaphylaxis: An updated practice parameter [Internet]. Vol. 115, Journal of Allergy and Clinical Immunology. Mosby Inc.; 2005 [cited 2020 May 11]. p. S483-523. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15753926

19. Kounis NG, Koniari I, Asimakopoulos S, Arumugham V, Saba L. The passepartout wayfares of Covid-19, Cytokine storm and Kounis syndrome. 2020 Aug 10 [cited 2020 Aug 13]; Available from: https://zenodo.org/record/3977924

20. Arumugham V. Vaccines and Biologics injury table based on mechanistic evidence – Feb 2020 Covering over 125 conditions [Internet]. 2020 [cited 2020 Apr 23]. Available from: https://doi.org/10.5281/zenodo.2582634

21. Arumugham V. Institute of Medicine: Most epidemiological vaccine safety studies are useless [Internet]. 2019 [cited 2019 Jun 12]. Available from: https://doi.org/10.5281/zenodo.3244496