Adjuvants for Pandemic Vaccines: Benefits and Challenges
High-level overview

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Adjuvants

- Added to a vaccine to improve the immune response
  - Increase antibody titers
  - Increase breadth of response
  - Provide appropriate bias (Th1 / Th2)
  - Induce cell-mediated immunity
  - Enable immunization in weakened immune system (e.g., geriatric)

- For pandemics: Reduce antigen dose, number of doses

- For recombinant vaccines generally a critical enabling component
Example: dose sparing for pandemic influenza vaccines

- Dose-sparing of antigen seen with o/w
  - 8-10 fold dose reduction for H5N1

- Incorporated in 2009 H1N1 pandemic vaccine
  - 2-4 fold dose sparing
  - Increase global vaccine production capacity
  - >200 million doses distributed for all ages
Adjuvants in approved routine vaccines

- Aluminium salts (alum): many vaccines

- Oil-in-water emulsions (eg MF59™, AS03™) in some seasonal influenza vaccines eg Fluad™.
  - Strong dose-reduction for pandemic influenza. Widely used in pH1N1 pandemic.

- Lipopolysaccharide derivatives (eg 3D-MPL, AS04) in Cervarix™

- Saponins (eg AS01, Matrix-M) in Mosquirix™, Shingrix™, R21,

- Oligonucleotides (eg CpG) in Heplisav™.

- Many other adjuvants under development…. 
Adjuvants in EUL approved covid vaccines

Adapted from Higdon M et al 2022 *Open Forum Infectious Diseases* doi: [10.1093/ofid/ofac138](https://doi.org/10.1093/ofid/ofac138)
Some challenges to using adjuvants during a pandemic…

- Is the adjuvant already in an approved vaccine?
  - If not is there extensive clinical data in different age-groups?

- Is GMP supply readily available?

- Compatible with co-formulation? Liquid?

- ....
Adjuvants are a lightning rod for public concerns...

Harmful adjuvant in swine influenza vaccine

Discussion

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Re. Klaus Larsen interview with Dr. Kan Mølbak in Ugeskrift for Doctors (2009, 171:2616). In the interview mentioned peripherally, that "the CSX vaccine, Denmark has commissioned, has an adjuvant. The EMEA says that danger can only be determined during and after mass vaccination.

Adjuvants are squalene, hajole. There are very strong indications that Gulf War syndrome from the first Gulf War (and later cases) just became - and remains - caused by squalene in anthrax vaccine for both deployed and hjemmestationerat U.S. military personnel.

Both groups - which excludes radiation as the cause - got the syndrome: inability to concentrate, allergies, polyarthritis, lymphomas, elevated ESR, fever, lupus erythematosus disseminated and MS, including In a few studies [1, 2] had the sick elevated antibody titres against squalene - which was not the case with the healthy. Professor R.F. Garry commented thereon to the U.S. Congress. U.S. Defense Department will not make a lot of study of squalenets