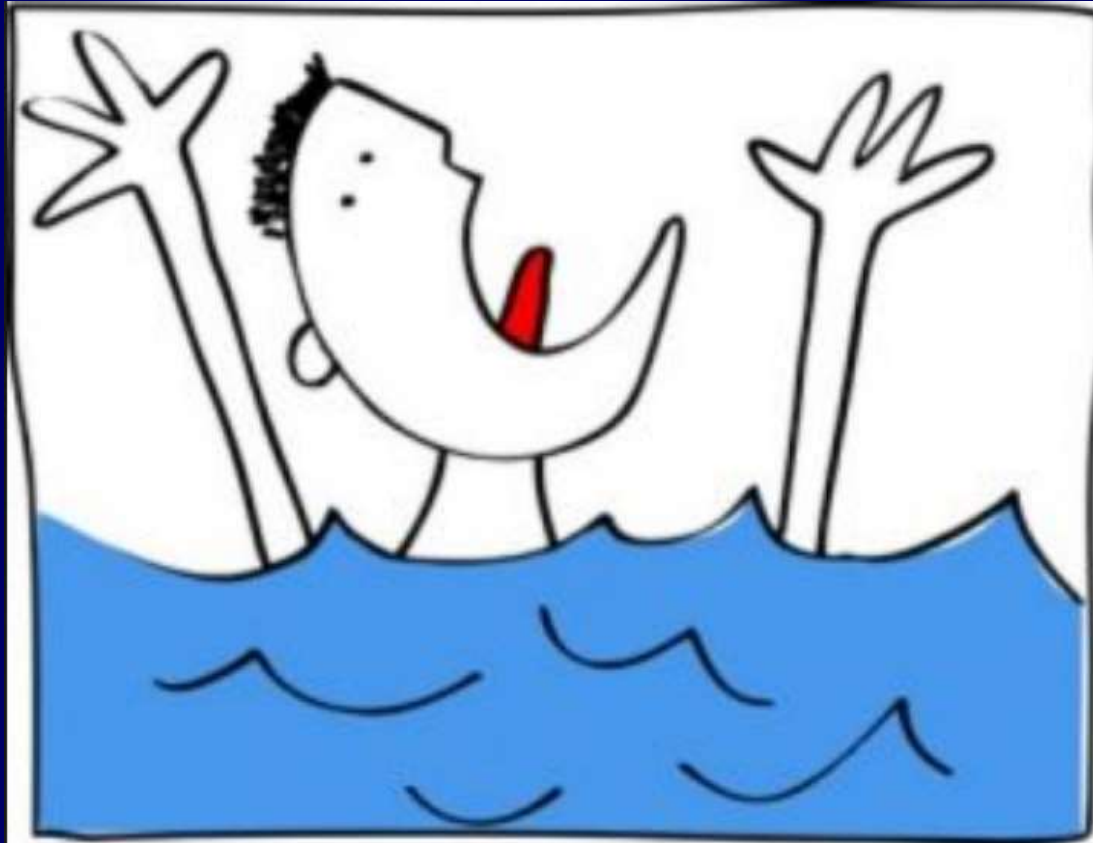


Vaccine Up-Date 2019

Family Medicine 2019



Lutheran Education SA,NT & WA

Brian J Ward

McGill Division of Infectious Diseases
Research Institute - McGill University Health Center

LEARNING OBJECTIVES

Outline broad changes in recent vaccines & vaccine use

Discuss how the vaccine environment is changing

Consider approaches to addressing vaccine controversies



Conflict of Interest Statement (Last 5 Years)

Position in Pharma	Medical Officer for Medicago Inc. (Oct 2011 - present)
Consulting	Pfizer, Merck, Novartis, GSK, Sanofi Pasteur MSSS, US Dept of Justice (Vaccine Compensation Programs)
Contracts	Vaccine trials for virtually all companies
Shared Awards	Shared CIHR Team grant (Laval U, GSK) CIHR-Industry grant (Medicago) Shared CQDM grant (Medicago, Laval J, SNC Lavalin)
Occasional Speakers Honoraria	Pfizer, Sanofi Pasteur, Novartis
Investments	None

Adjuvants



upstartHR



Dhaka Tribune

Historically

Aluminum salts



IndiaMART

Progress

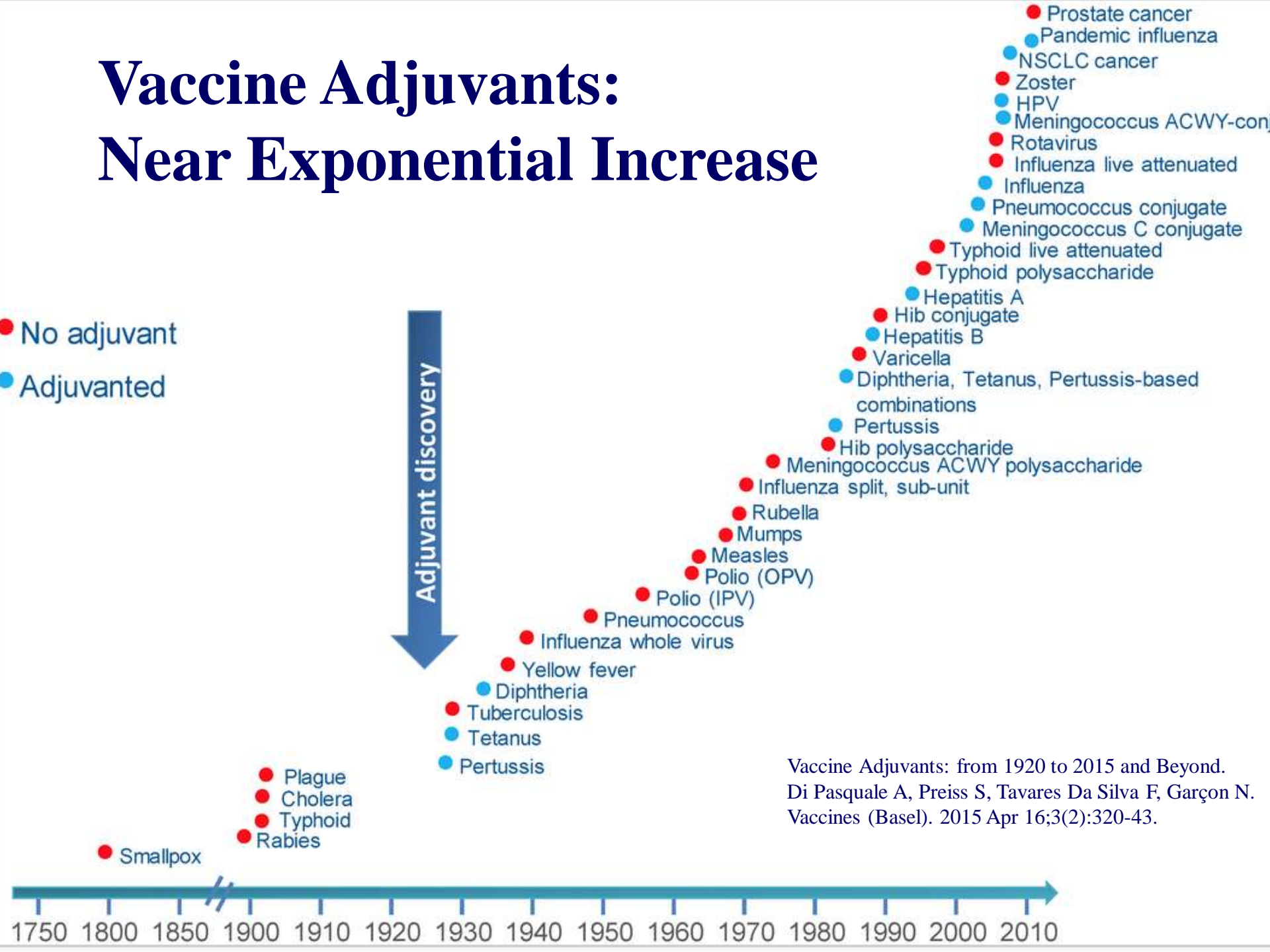
MF-59 (oil-in-water: squalene) – FluAd™
MPLA – Human Papillomavirus (Cervarix™)
CpG 1018 – Hepatitis B (Heplisav™)
ASO1b (MPLA/QS-21) – Shingles (Shingrix™)
ASO3 (squalene+vitamin E – pdm Influenza

Research

GSK: AS series	IMV:DPX (DepoVax)
Sanofi: AF series	Papaya mosaic virus
IDRI: GLA-SE/AF	Chitosan

QS - Quillaja saponaria
MPLA - Monophosphoryl lipid A

Vaccine Adjuvants: Near Exponential Increase



Vaccine Adjuvants: from 1920 to 2015 and Beyond.
 Di Pasquale A, Preiss S, Tavares Da Silva F, Garçon N.
 Vaccines (Basel). 2015 Apr 16;3(2):320-43.

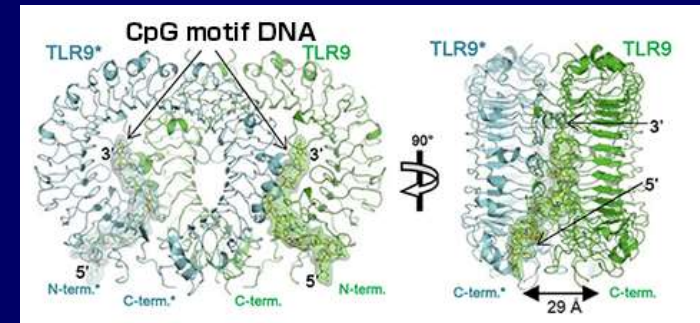
CpG Adjuvanted HBV Vaccine



HBs antigen + CpG ODN 1018
Activates TLR9

February 2018

- FDA announced licensure of 2-dose schedule
- A better vaccine for adults including those with medical problems
- Licensure delayed by adjuvant



A screenshot of a journal article page from Elsevier. The page title is 'Vaccine' and the journal is 'Vaccine 36 (2018) 668-674'. The article title is 'Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults'. The authors listed are Sam Jackson, Joseph Lentino, James Kopp, Linda Murray, William Ellison, Margaret Rhee, Gerald Shockey, Lalith Akella, Kimberly L. Heyward, and Robert S. Janssen. The Elsevier logo is visible on the left, and a 'Vaccine' logo is on the right.

First use of a CpG adjuvant in humans



Conflicting Messages



Innocent and carefree, Stuart's left hand didn't know what the right was doing

- One branch of the Canadian government gives 'nosodes' (homeopathic vaccines) a registration number while another states that they don't work
- One province gives the second dose of MMR at 12 months while another gives it at 4-6 years of age
- There is often no consistency on vaccine use on the Ottawa versus the Gatineau side of the Ottawa River (for example)



Problems with Product Monographs (Influenza)

Fluzone Quadrivalent

Pregnant Women

Animal reproductive studies have not been conducted with FLUZONE[®] Quadrivalent. It is also not known whether FLUZONE[®] Quadrivalent can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

Data on the use of this vaccine in pregnant women are limited. FLUZONE[®] Quadrivalent should be given to pregnant women only if clearly needed and following an assessment of the risks and benefits. However, there is no evidence to suggest a risk to the fetus or the pregnancy from maternal immunization with FLUZONE[®] Quadrivalent. (2)

NACI states that influenza vaccination is recommended for pregnant women. (2)

FluLaval Tetra

Pregnant Women: The safety of FLULAVAL TETRA when administered to pregnant women has not been evaluated. Animal studies with FLULAVAL TETRA do not indicate direct or indirect harmful effects with respect to reproductive and developmental toxicity. FLULAVAL TETRA should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.

Influenza (2017-2019)



MIT Mathematics

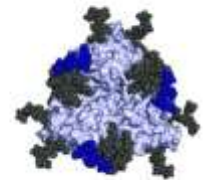
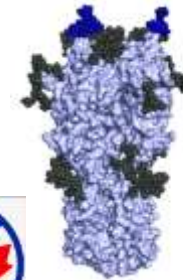
- **Live Attenuated Influenza Vaccine**
 - Low efficacy in the USA (H1N1pdm) 2013/14, 2015/16
 - Initially thought to be when 4th virus added
 - ACIP flip-flopped → low replication of cold-adapted H1N1pdm
- **First recombinant vaccine (HA)**
 - 45mg of each strain with no adjuvant
 - more effective in subjects >50 years old
- **2017-2018 egg-based mismatch for H3N2**
 - H3N2 grown in eggs → mutations
 - Low vaccine efficacy ~10% - worst season in 10-15 years
 - Cell-based vaccine (eg: Flucelvax™) worked ~10% better
- **2018-2019 another mismatch H3N2**
 - Longest season in a decade – moderate intensity
- **2019-2020 – problems with H3N2 & B_{Victoria}**
 - Early start to season in Australia with high severity
 - Starting early in the USA



Protein Scier
CORPO

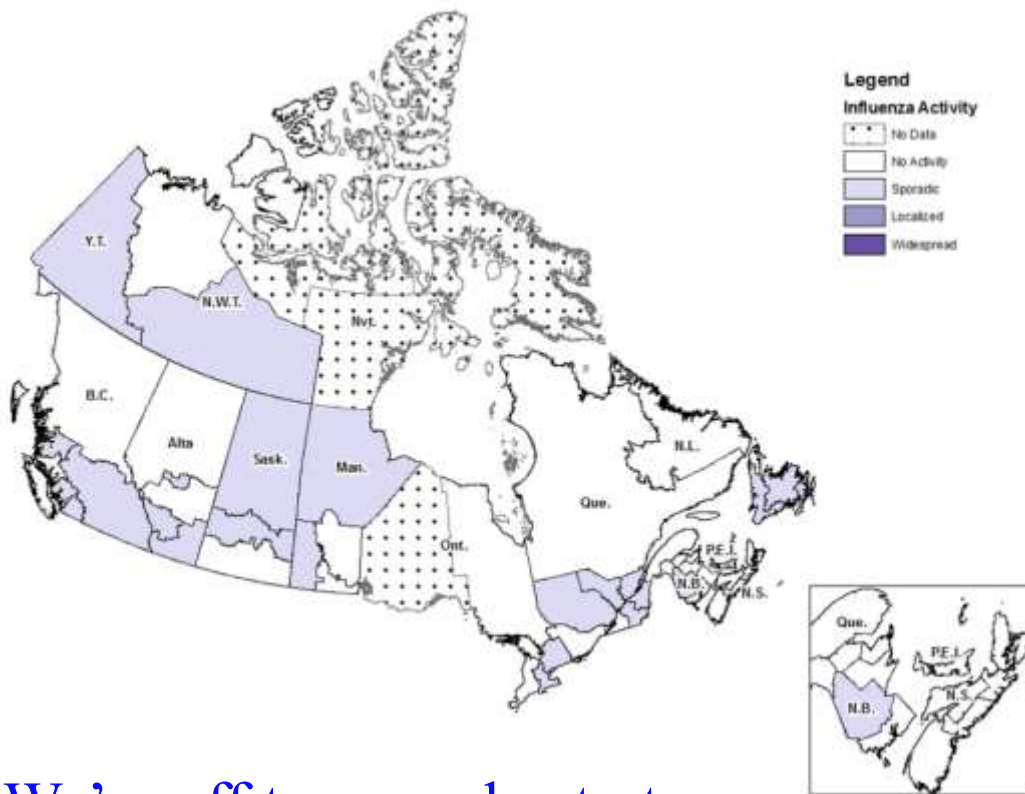


Makers of **Flublok**[®]
Influenza vaccine



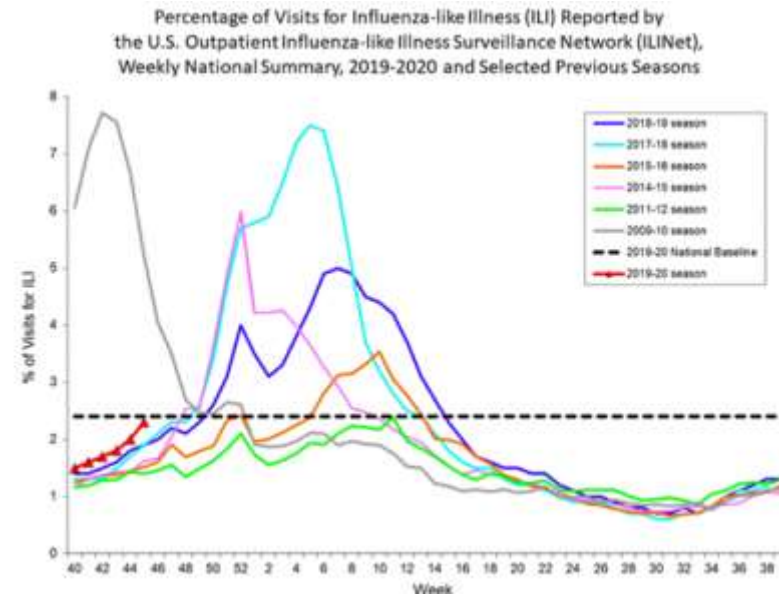
Influenza (2019-2020)

Week of November 11-17, 2019



We're off to an early start
H3N2 in the elderly (~75%)
B strains in the young

Same pattern in the USA
Early start
Mix of H1N1, H3N2 and
two different B strains



Mixed & Shortened Vaccine Schedules

- An issue since the first multi-dose schedules introduced
- Added complexity with ‘non-identical’ vaccines
 - Hib conjugates (TT, dT, OMP)
 - Different serotypes/genotype/adjuvants
- How many doses – for society or for the individual?

Shortened Schedules



Quebec has played a major international role in reduced-dose schedules for several vaccines

Concept of ‘marginal benefit’

Mixed Schedules



Quebec is now playing a major national (and possibly international) role spearheading the use of mixed schedules

Concept of ‘synergistic benefit’

Reduced Dose Schedules

Benefits of Booster Doses

Tetanus – do we really need a booster every ten years?

HBV – does everyone need 3 doses of HBV?
- boosters for those at high risk?

Pneumococcus – how many doses of PCVs (young/old)?
- booster doses for PS vaccine (old)?

HPV – how many doses?
- booster doses?

HAV – how many doses?
- booster doses?



Vaccine
Volume 23, Issue 31, 1 July 2005, Pages 4082-4087



Immunogenicity of two paediatric doses of monovalent hepatitis B or combined hepatitis A and B vaccine in 8–10-year-old children

Bernard Duval^{a, b, c, d, e, f}, Vladimir Gilca^b, Nicole Boulianne^{a, b}, Genevieve Deceuninck^b, Louis Rochette^a, Gaston De Serres^{a, b, c}

Good Reasons for More Doses

- Better individual protection
- Better population protection
(ie: fewer vaccine failures)
- Longer duration of protection



Community Links

Bad Reasons for More Doses

- More profit for industry
- It's fun to stick people with needles
- Our vaccines aren't good enough
- Because we haven't studied fewer doses



Dreamstime.com

Mixed Schedules

- Logistically more challenging
 - ordering & storage
 - record keeping
 - increased complexity throughout
- Likelihood of errors increased
 - is the order important?
- Who pays for mixed-schedule studies

What's the Best HPV Vaccination Schedule?

Personal Opinion

Two doses of Merck 9-valent vaccine

+

One dose of GSK bi-valent vaccine



Pre-Puberty



[Whats-Happening-Tom-conditions-Sexuality/dp/1849055238](https://www.pinterest.com/pin/1849055238/)

Gardasil™

(+) targets 9 HPV genotypes

(-) weaker adjuvant (alum)

Cervarix™

(+) stronger adjuvant (ASO4)

(-) targets only 2 HPV genotypes

Mandatory Vaccines

Measles at School-entry in Ontario



Influenza In HCW



<http://rpmdaily.net/blog/i-always-wondered-why-people-say-god-bless-you-when-you-sneeze-now-i-know>



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PLoS One. 2017; 12(1): e0163586.

PMCID: PMC5271324

Published online 2017 Jan 27. doi: [10.1371/journal.pone.0163586](https://doi.org/10.1371/journal.pone.0163586)

PMID: [28129360](https://pubmed.ncbi.nlm.nih.gov/28129360/)

Influenza Vaccination of Healthcare Workers: Critical Analysis of the Evidence for Patient Benefit Underpinning Policies of Enforcement

[Gaston De Serres](#),^{#1,2,*} [Danuta M. Skowronski](#),^{#3,4} [Brian J. Ward](#),⁵ [Michael Gardam](#),⁶ [Camille Lemieux](#),⁶ [Annalee Yassi](#),⁴ [David M. Patrick](#),^{3,4} [Mel Krajden](#),^{3,4} [Mark Loeb](#),⁷ [Peter Collignon](#),^{8,9} and [Fabrice Carrat](#)^{10,11,12}

2017-2018: A Regrettable Milestone



European Centre for Disease Prevention and Control
An agency of the European Union

All topics: A to Z News & events Publications & data Tools About us Q

Home > News & events > Measles outbreaks still ongoing in 2018 and fatalities reported from four countries

< News & events

Measles outbreaks still ongoing in 2018 and fatalities reported from four countries

9 Mar 2018

Measles cases spike globally due to gaps in vaccination coverage

<https://www.who.int/news-room/detail/29-11-2018-measles-cases-spike-globally-due-to-gaps-in-vaccination-coverage>

<https://ecdc.europa.eu/en/news-events/measles-outbreaks-still-ongoing-2018-and-fatalities-reported-four-countries>

- Measles cases increase 30% from 2016 to 2017
 - >110,000 children died from measles
 - Americas, Eastern Mediterranean and Europe
- >14,500 cases with 57 deaths
Most in Romania (5,224), Italy (4,978), Greece (1,398) and Germany (906),

Careful Communication



Stop the hysteria over measles outbreaks

NEIL RAU AND RICHARD SCHABAS

CONTRIBUTED TO THE GLOBE AND MAIL

PUBLISHED OCTOBER 2, 2018

UPDATED OCTOBER 3, 2018

PUBLISHED OCTOBER 2, 2018

This article was published more than 1 year ago. Some information in it may no longer be current.

- The authors are correct but the opinion piece is not helpful
- The sky is not falling ... there is no tsunami of measles cases coming ... but far too many Canadians are susceptible and the % is increasing

Risk in Perspective

‘Measles is not that dangerous ...’



“If you were going to Canada’s Wonderland, and they said, ‘It’s a really safe ride but every 3,000-5,000 rides, someone is going to die,’ nobody would get on that ride.”

Un professeur de l'UQTR multiplie les propos anti-vaccins



PHOTOMONTAGE LA PRESSE

Au moment où la ville de New York tente d'endiguer une épidémie de rougeole et alors que les autorités de santé publique du Canada disent vouloir agir contre le mouvement anti-vaccins, un professeur de biochimie de l'Université du Québec à Trois-Rivières, Christian Linard, multiplie les propos contre la vaccination sur sa page Facebook personnelle. Une situation dénoncée par plusieurs intervenants.

Publié le 12 avril 2019 à 5h00



PHILIPPE MERCURE
LA PRESSE

Des publications « irresponsables »

Quebec is not 'Immune' to anti-Vax Nonsense



Christian Linard

28 février, à 04 h 25 · 🌐

De 1993 à 2014 au Kenya, le vaccin anti-tétanique contenait aussi l'antigène HCG (humain chorionique gonadotrope humaine). Pourquoi?

Pour stériliser massivement les femmes kényanes sans leur consentement.

Peux t'on se fier à nos gouvernements? À nos organismes de santé publique? Aux compagnies pharmaceutiques?... [Afficher la suite](#)

SCIRP.ORG

HCG Found in WHO Tetanus Vaccine in Kenya Raises Concern in the Developing World

In 1993, WHO announced a "birth-control vaccine" for "family planning". Published research shows that by 1976 WHO researchers had conjugated tetanus toxoid (TT) with human chorionic gonadotropin (hCG) producing a...

Vaccine Ingredients

Formaldehyde

Aluminum

Thimerosal (influenza vaccines)

Polysorbate 80

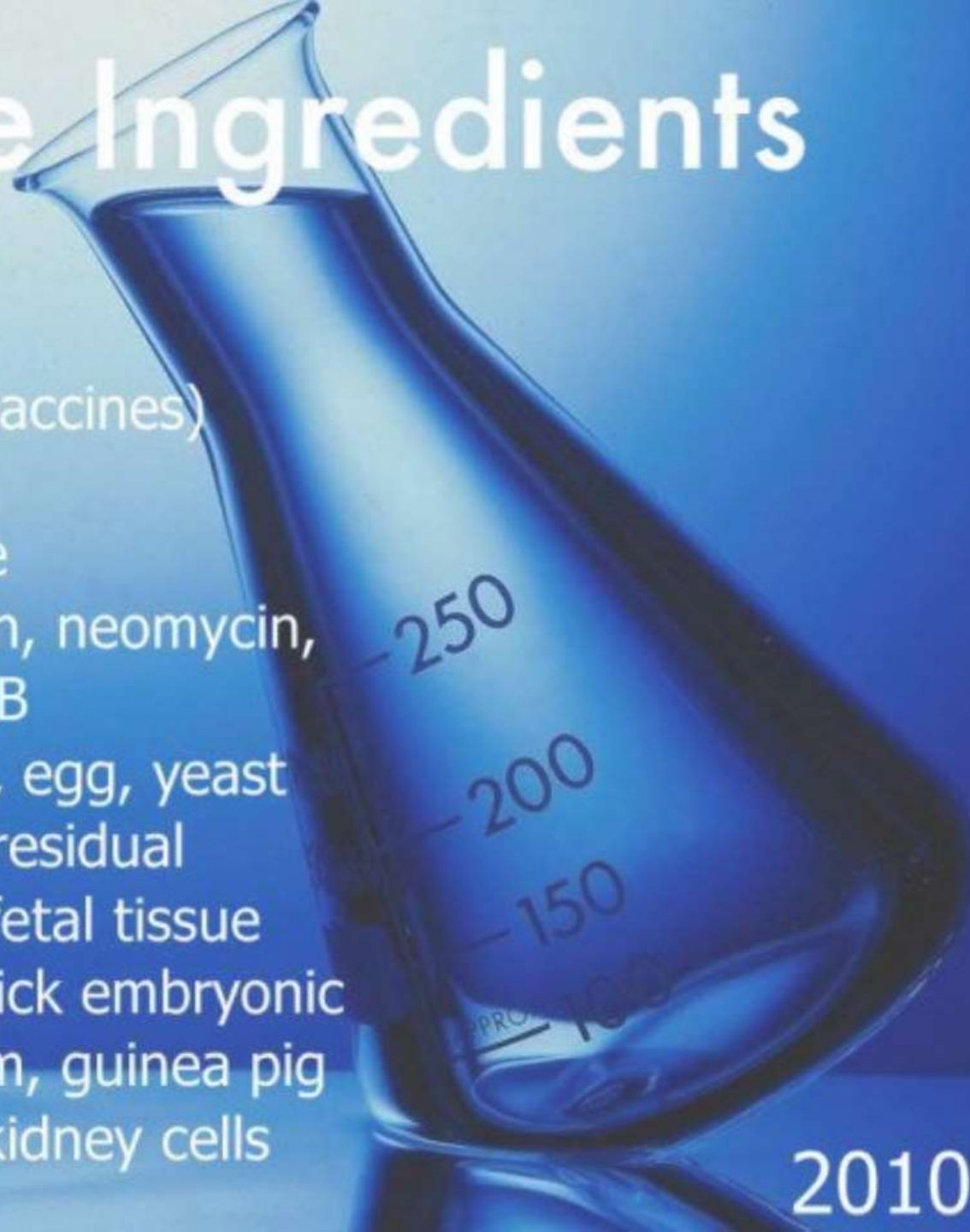
Monosodium Glutamate

Antibiotics: streptomycin, neomycin,
gentamicin, polymyxin B

Allergens: soy, gelatin, egg, yeast

Human diploid cells or residual
proteins from aborted fetal tissue

Animal by products: chick embryonic
fluid, fetal bovine serum, guinea pig
embryo cells, monkey kidney cells



Fighting Back

Is one of these things *not* like the other?



This is the formaldehyde in a vaccine



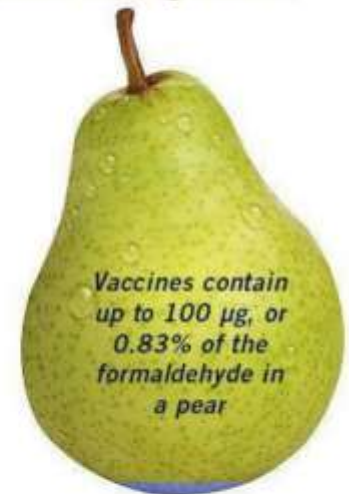
This is the formaldehyde which your own body makes

One carbon atom, two hydrogen atoms and one oxygen atom.
Formaldehyde is formaldehyde.

Concerned about formaldehyde in vaccines? Consider the pear...



A 200 g pear contains up to 12,000 µg of formaldehyde, naturally



Vaccines contain up to 100 µg, or 0.83% of the formaldehyde in a pear

The amount of formaldehyde in a vaccine is so tiny that it doesn't even affect the naturally occurring levels of formaldehyde in a child's blood.

Source: <http://tinyurl.com/foodCH20>



For Jude ...



<https://www.youtube.com/watch?v=bpkuuVNF1AI>

Mumps



www.cbc.ca

Triple Threat

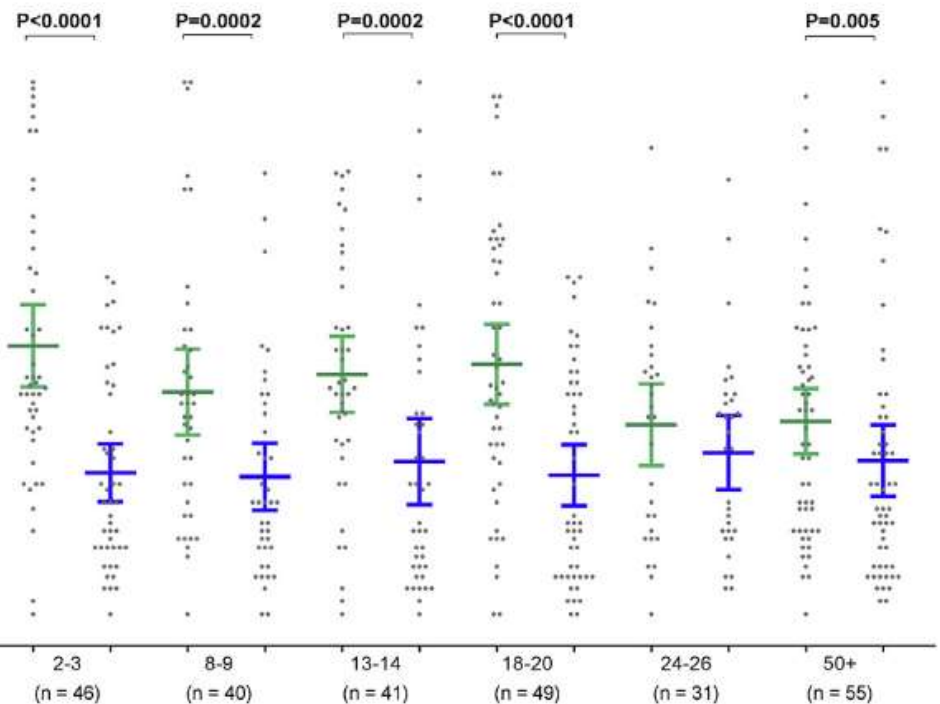
- 1) Waning Immunity (like measles)
- 2) Under vaccination
- 3) Vaccine hesitancy (because of measles and MMR)
- 4) Shifting genotype

Genotype A
(Jeryl Lynn)

Genotype G
(Circulating viruses)

neutralizing titre

500
90
9 = cut-off



Vermeire T, et al. Sera from different age cohorts in Belgium show limited cross-neutralization between the mumps vaccine and outbreak strains. Clin Microbiol Infect. 2018:S1198-743X(18)30743-2.

Streptococcus pneumoniae



radiopaedia.org

Prevnar 13



<http://neatorama.cachefly.net/images/2007-08/sumo-kid.jpg>

*One of most profitable
global pharma products*

Pharma ‘Hard-Ball’

- Adult pneumococcal vaccine a ‘numbers game’
- First had 23-valent polysaccharide vaccine
- Then pediatric conjugate vaccines

- 7-valent



- 10 valent



- 13 valent



- 15-valent



(soon)

- Pfizer: secure Canadian market just before 15-valent arrives
- Provinces convulsed around issue of ‘mixed’ vaccine schedules schedules and desire of companies to maintain/gain market-share
- Quebec the only province to refuse multi-year ‘deal’ on 13-valent vaccine on the eve of licensure of the 15-valent product
- This wheeling & dealing explains Quebec’s seemingly paradoxical recommendation for the 10-valent product

Current Vaccine Shortages & Delays



Vaccine Shortages



White paper: Medicine and vaccine shortages

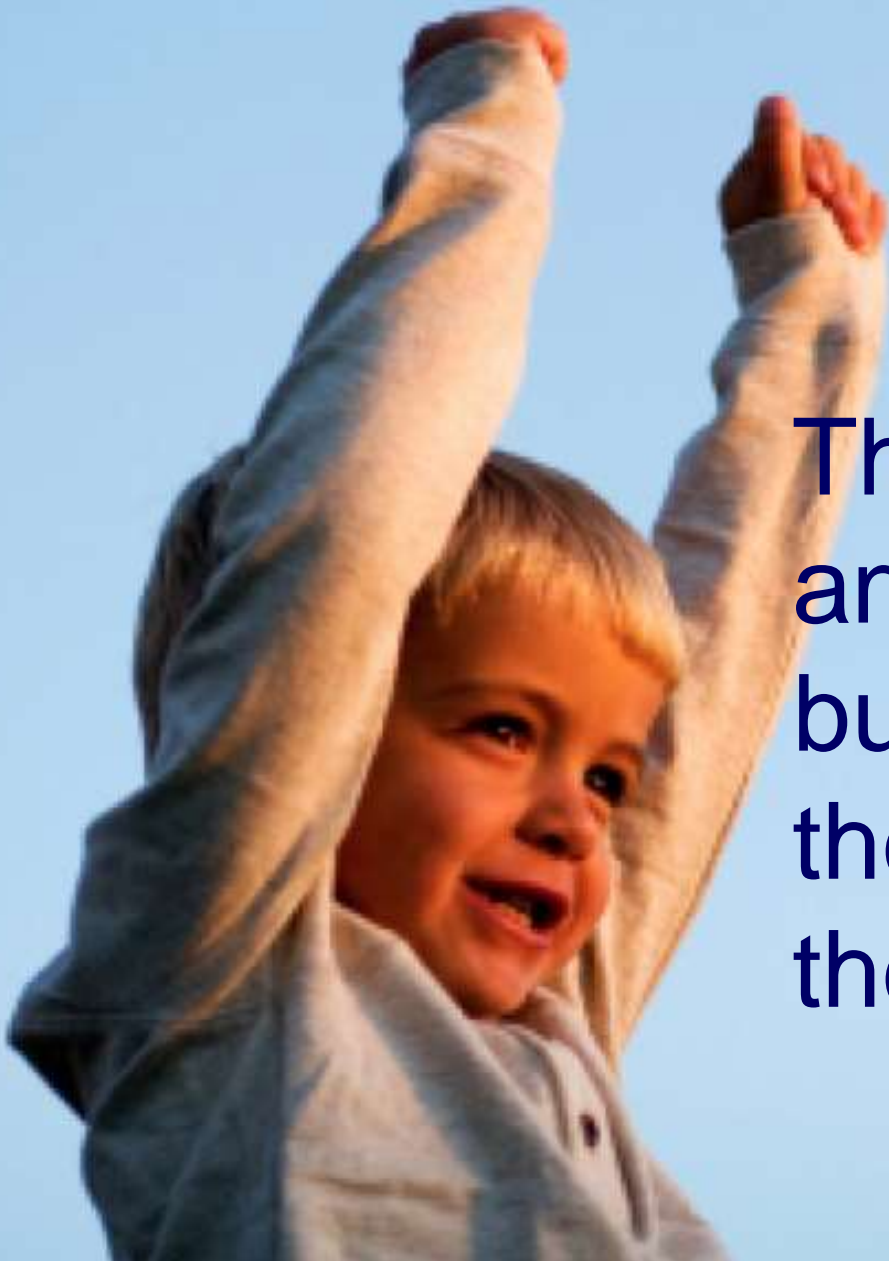
June 19th 2018 | Multiple countries | Pharmaceuticals and biotechnology

Medicines and vaccine shortages affect rich and poor countries alike, finds a [new EIU report](#). However, finding a solution may be difficult.

- long considered a LMIC problem, stock-outs and back-orders now common in even wealthiest countries
- 25% of stock-outs in last few years have occurred in rich countries
- on-going shortages of hepatitis A and B vaccines
- continuing shortage of yellow fever vaccines
- chronic shortages of rabies vaccines and rabies immune globulin

Many of our vaccines made in only 1 factory

Bad luck, re-tooling, changing priorities, surge demand



There are concerns
and problems
but I'm an optimist ..
the more vaccines
the better!