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## **Exemptions and Immunity**

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## Medical and Nonmedical Exemptions and Immunity Documentation

By far, parents in Oregon vaccinate their children. Parents who cannot or do not want their children to be vaccinated can claim an exemption for one or all school immunizations

(/oha/PH/PREVENTIONWELLNESS/VACCINESIMMUNIZATION/GETTINGIMMUNIZED/Pages/school.aspx). There two types of exemptions; medical and nonmedical. In addition, some people may show immunity because of having had a disease or with a blood test. See below for explanations, directions and required forms for completing the exemption process.

## Medical Exemptions

Some people cannot get immunized because of a medical reason. Physicians can sign medical exemptions for children with valid contraindications (https://www.cdc.gov/vaccines/hcp/acip-recs/generalrecs/contraindications.html) to an immunization as determined by the Advisory Committee on Immunization Practices.

There are two kinds of medical exemptions, temporary and permanent. Temporary medical exemptions are given an expiration date after which the child will need to receive the vaccine, or the physician will need to write a request for an extension for re-review by the local health department. With a permanent medical exemption, the child will never be required to receive the vaccine.

To apply for a medical exemption for a child, the parent must submit a letter signed by a licensed physician stating:

- Child's name
- Birth date
- Medical condition that contraindicates vaccine
- List of vaccines contraindicated
- Approximate time until the condition resolves, if applicable
- Physician's signature
- Physician's contact information including the phone number

## Nonmedical Exemptions

Some people choose not to vaccinate for personal, religious, or philosophical reasons and they can claim a nonmedical exemption to some or all immunizations. To claim a nonmedical exemption for children in child care, preschool, K-12, or college, visit healthoregon.org/vaccineexemption (http://healthoregon.org/vaccineexemption).

## Immunity Documentation

If a person can show immunity to certain diseases they do not need to provide vaccination dates. Immunity documentation is acceptable for history of disease or positive titer (blood test) for hepatitis B, hepatitis A, Hib, MMR or varicella. Immunity documentation is not acceptable for diphtheria, tetanus, pertussis or polio.

To submit immunity documentation for a child, the parent must have a letter or lab test from a licensed physiolan stating:

- · Child's name
- Birth date
- Diagnosis or lab report

Parents can sign for history of disease for varicella.

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## **Contraindications and Precautions**

General Best Practice Guidelines for Immunization: Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)

Printer friendly version [18 pages]

## Updates

Major changes to the best practice guidance in this section include 1) enhancement of the definition of a "precaution" to include any condition that might confuse diagnostic accuracy and 2) recommendation to vaccinate during a hospitalization if a patient is not acutely moderately or severely ill.

## **General Principles**

Contraindications (conditions in a recipient that increases the risk for a serious adverse reaction) and precautions to vaccination are conditions under which vaccines should not be administered. Because the majority of contraindications and precautions are temporary, vaccinations often can be administered later when the condition leading to a contraindication or precaution no longer exists. A vaccine should not be administered when a contraindication is present; for example, MMR vaccine should not be administered to severely immunocompromised persons (1). However, certain conditions are commonly misperceived as contraindications (i.e., are not valid reasons to defer vaccination).

National standards for pediatric vaccination practices have been established and include descriptions of valid contraindications and precautions to vaccination (2). Persons who administer vaccines should screen patients for contraindications and precautions to the vaccine before each dose of vaccine is administered (Table 4-1). Screening is facilitated by consistent use of screening questionnaires, which are available from certain state vaccination programs and other sources (e.g., the Immunization Action Coalition (http://www.immunize.org) ).

Severely immunocompromised persons generally should not receive live vaccines (3). Because of the theoretical risk to the fetus, women known to be pregnant generally should not receive live, attenuated virus vaccines (4). Persons who experienced encephalopathy within 7 days after administration of a previous dose of pertussis-containing vaccine not attributable to another identifiable cause should not receive additional doses of a vaccine that contains pertussis (4,5). Severe Combined Immunodeficiency (SCID) disease and a history of intussusception are both contraindications to the receipt of rotavirus vaccines  $(\underline{6})$ .

A precaution is a condition in a recipient that might increase the risk for a serious adverse reaction, might cause diagnostic confusion, or might compromise the ability of the vaccine to produce immunity (e.g., administering measles vaccine to a person with passive immunity to measles from a blood transfusion administered up to 7 months prior) (Z). A person might experience a more severe reaction to the vaccine than would have otherwise been expected; however, the risk for this happening is less than the risk expected with a contraindication. In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution if the benefit of protection from the vaccine outweighs the risk for an adverse reaction.

The presence of a moderate or severe acute illness with or without a fever is a precaution to administration of all vaccines (Table 4-1). The decision to administer or delay vaccination because of a current or recent acute illness depends on the severity of symptoms and etiology of the condition. The safety and efficacy of vaccinating persons who have mild illnesses have been documented (8-11). Vaccination should be deferred for persons with a moderate or severe acute illness. This precaution avoids causing diagnostic confusion between manifestations of the underlying illness and possible adverse effects of vaccination or superimposing adverse effects of the vaccine on the underlying illness. After they are screened for contraindications, persons with moderate or severe acute illness should be vaccinated as

soon as the acute illness has improved. Studies indicate that failure to vaccinate children **w**ith minor illnesses can impede vaccination efforts (<u>12–14</u>). Among persons whose compliance with medical care cannot be ensured, use of every opportunity to administer appropriate vaccines is critical.

Hospitalization should be used as an opportunity to provide recommended vaccinations. Health-care facilities are held to standards of offering influenza vaccine for hospitalized patients, so providers are incentivized to vaccinate these patients at some point during hospitalization (15). Likewise, patients admltted for elective procedures will not be acutely ill during all times during their hospitalization. Most studies that have explored the effect of surgery or anesthesia on the immune system were observational, included only infants and children, and were small and indirect, in that they did not look at the immune effect on the response to vaccination specifically (16-35). They do not provide convincing evidence that recent anesthesia or surgery significantly affect response to vaccines. Current, recent, or upcoming anesthesia/surgery/hospitalization is not a contraindication to vaccination (16-35). Efforts should be made to ensure vaccine administration during the hospitalization or at discharge. For patients who are deemed moderately or severely ill throughout the hospitalization, vaccination should occur at the earliest opportunity (i.e., during immediate post-hospitalization follow-up care, including home or office visits) when patients' clinical symptoms have improved.

A personal or family history of seizures is a precaution for MMRV vaccination; this is because a recent study found an increased risk for febrile seizures in children 12-23 months who receive MMRV compared with MMR and varicella vaccine (<u>36</u>).

Clinicians or other health-care providers might misperceive certain conditions or circumstances as valid contraindications or precautions to vaccination when they actually do not preclude vaccination (2) (Table 4-2). These misperceptions result in missed opportunities to administer recommended vaccines (37).

Routine physical examinations and procedures (e.g., measuring temperatures) are not prerequisites for vaccinating persons who appear to be healthy. The provider should ask the parent or guardian if the child is ill. If the child has a moderate or severe illness, the vaccination should be postponed.

Vaccine	Citation	Contraindications	Precautions
DT, Td	( <u>4</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	GBS <6 weeks after previous dose of tetanus-toxoid- containing vaccine History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoidcontaining or tetanus- toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid-containing vaccine Moderate or severe acute illness with or without fever
DTaP	( <u>38</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, <b>w</b> ithin 7 days of administration of previous dose of DTP or DTaP	<ul> <li>Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy; defer DTaP until neurologic status clarified and stabilized</li> <li>GBS &lt;6 weeks after previous dose of tetanus-toxoid-containing vaccine</li> <li>History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid-containing or tetanus-toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid-containing vaccine</li> <li>Moderate or severe acute illness with or without fever</li> </ul>
Hepatitis A	( <u>39</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a	Moderate or severe acute illness with or without fever

## TABLE 4-1. Contraindications and precautions<sup>(a)</sup> to commonly used vaccines

		vaccine component	
Hepatitis B	( <u>40</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Hypersensitivity to yeast	Moderate or severe acute illness with or without fever
Hib	( <u>41</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Age <6 <b>w</b> eeks	Moderate or severe acute illness with or without fever
HPV	( <u>42</u> )	Severe allergic reaction (e.g.,	Pregnancy
		anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
IIV	( <u>43</u> )	Severe allergic reaction (e.g.,	GBS <6 weeks after a previous dose of influenza vaccine
		anaphylaxis) after previous dose of influenza vaccine or to vaccine	Moderate or severe acute illness with or without fever
		component.	Egg allergy other than hives, e.g., angioedema, respiratory distress, lightheadedness, recurrent emesis; or required epinephrine or another emergency medical intervention (IIV may be administered in an inpatient or outpatient medical setting and under the supervision of a health care provider who is able to recognize and manage severe allergic conditions).
IPV	( <u>44</u> )	Severe allergic reaction (e.g.,	Pregnancy
		anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
LAIV <sup>(b)</sup>	( <u>43</u> )	Severe allergic reaction (e.g., anaphylaxis) after a vaccine component, including egg protein Concomitant use of aspirin or aspirin-	GBS <6 weeks after a previous dose of influenza vaccine Asthma in persons aged 5 years old or older Medical conditions which might predispose to higher risk of
		containing medication in children and adolescents	complications attributable to influenza <sup>(c)</sup>
		LAIV4 should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours	Moderate of severe acute illness with or without fever
MenACWY	( <u>45</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
MenB	( <u>46, 47</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
MMR <sup>(d),(e)</sup>	(1)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Pregnancy	Recent (≤11 months) receipt of antibody-containing blood product (specific interval depends on product) History of thrombocytopenia or thrombocytopenic purpuraNeed for tuberculin skin testing or interferon-gamma release assay (IGRA) testing <sup>(h)</sup>
			Moderate or severe acute illness with or without fever

Moderate or severe acute illness with or without fever

		Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy <sup>(f)</sup> or patients	
		with HIV infection who are severely immunocompromised) Family history of altered immunocompetence <sup>(g)</sup>	
MPSV4	( <u>48</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
PCV13	( <u>49</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose of PCV13 or any diphtheria-toxoid– containing vaccine or to a component of a vaccine (PCV13 or any diphtheria- toxoid–containing vaccine)	Moderate or severe acute illness with or without fever
PPSV23	( <u>50</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
RIV	( <u>43</u> )	Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine	GBS <6 weeks after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever
Rotavirus	( <u>6</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component SCID	Altered immunocompetence other than SCID Chronic gastrointestinal disease <sup>(i)</sup> Spina bifida or bladder exstrophy <sup>(i)</sup> Moderate or severe acute illness <b>w</b> ith or <b>w</b> ithout fever
		History of intussusception	Moderate of severe acute liness with or without rever
Tdap	( <u>51</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another	GBS <6 weeks after a previous dose of tetanus-toxoid– containing vaccine Progressive or unstable neurological disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized
		identifiable cause, <b>w</b> ithin 7 days of administration of previous dose of DTP, DTaP, or Tdap	History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid—containing or tetanus- toxoid–containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid–containing vaccine
			Moderate or severe acute illness with or without fever
Varicella <sup>(d),</sup> (e)	( <u>52</u> )	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Known severe immunodeficiency (e.g., from hematologic and solid tumors,	Recent (≤11 months) receipt of antibody-containing blood product (specific interval depends on product) Moderate or severe acute illness with or without fever
		receipt of chemotherapy, congenital	Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination (avoid use of these

immunodeficiency, long-term immunosuppressive therapy<sup>(f)</sup> or patients with HIV infection who are severely immunocompromised)(e)

Pregnancy

Family history of altered immunocompetence<sup>(g)</sup>

Zoster

(53)

Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy<sup>(f)</sup> or patients with HIV infection who are severely immunocompromised)(e)

antiviral drugs for 14 days after vaccination)

Use of aspirin or aspirin-containing products<sup>(j)</sup>

Moderate or severe acute illness with or without fever

Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination (avoid use of these antiviral drugs for 14 days after vaccination)

Pregnancy

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; DTP = diphtheria toxoid, tetanus toxoid, and pertussis; GBS = Guillain-Barré syndrome; Hib = Haemophilus influenzae type b; HIV = human immunodeficiency virus; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; SCID = severe combined immunodeficiency; RIV=recombinant influenza vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

(a) Events or conditions listed as precautions should be reviewed carefully. Benefits of and risks for administering a specific vaccine to a person under these circumstances should be considered. If the risk from the vaccine is believed to outweigh the benefit, the vaccine should not be administered. If the benefit of vaccination is believed to outweigh the risk, the vaccine should be administered. Whether and when to administer DTaP to children with proven or suspected underlying neurologic disorders should be decided on a case-by-case basis.

(b) In addition, ACIP recommends LAIV not be used for pregnant women, immunosuppressed persons, persons with egg allergy, and children aged 2-4 years who have asthma or who have had a wheezing episode noted in the medical record within the past 12 months, or for whom parents report that a health-care provider stated that they had wheezing or asthma within the last 12 months. LAIV should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours. Persons who care for severely immunosuppressed persons who require a protective environment should not receive LAIV, or should avoid contact with such persons for 7 days after receipt.

## (c) Source: (52).

(d) HIV-infected children may receive varicella vaccine if CD4+ T-lymphocyte count is ≥15% and should receive MMR vaccine if they are aged ≥12 months and do not have evidence of current severe immunosuppression (i.e., individuals aged <5 years must have CD4+T lymphocyte [CD4] percentages ≥15% for ≥6 months; and individuals aged >5 years must have CD4+percentages >15% and CD4+>200 lymphocytes/mm<sup>3</sup> for >6 months) or other current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those older than age 5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged <5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥6 months above age-specific CD4+count criteria: CD4+count >750 lymphocytes/mm<sup>3</sup> while aged ≤12 months and CD4+count ≥500 lymphocytes/mm<sup>3</sup> while aged 1 through 5 years. Sources: (1, 50).

(e) MMR and varicella-containing vaccines can be administered on the same day. If not administered on the same day, these vaccines should be separated by at least 28 days.

(f) A substantially immunosuppressive steroid dose is considered to be >2 weeks of daily receipt of 20 mg or 2 mg/kg body weight of prednisone or equivalent.

(8) family history of congenital or hereditary immunodeficiency in first-degree relatives (e.g., parents and siblings), unless the immune competence of the potential vaccine recipient has been substantiated clinically or verified by a laboratory.

(h) If active tuberculosis is suspected, MMR should be delayed. Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin or IGRA testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for  $\geq$ 4 weeks after the vaccination. If an urgent need exists to skin test or IGRA, do so with the understanding that reactivity might be reduced by the vaccine.

<sup>(i)</sup> For details, see (<u>55</u>).

<sup>(1)</sup>No adverse events associated with the use of aspirin or aspirin-containing products after varicella vaccination have been reported; however, the vaccine manufacturer recommends that vaccine recipients avoid using aspirin or aspirin-containing products for 6 weeks after receiving varicella vaccines because of the association between asplrIn use and Reye syndrome after varicella. Vaccination with subsequent close monitoring should be considered for children who have rheumatoid arthritis or other conditions requiring therapeutic aspirin. The risk for serious complications associated with aspirin is likely to be greater in children in whom natural varicella develops than it is in children who receive the vaccine containing attenuated VZV. No association has been documented between Reye syndrome and analgesics or antipyretics that do not contain aspirin."

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## TABLE 4-2. Conditions incorrectly perceived as contraindications or precautions to vaccination (i.e., vaccines may be given under these conditions)

Vaccine	Conditions commonly misperceived as contraindications or precautions
General for all vaccines, including DTaP, pediatric DT, adult Td, adolescent-adult Tdap, IPV, MMR, Hib, hepatitis A, hepatitis B, varicella, rotavirus, PCV13, IIV, LAIV, PPSV23, MenACWY, MPSV4, HPV, and herpes zoster	Mild acute illness with or without fever Lack of previous physical examination in well-appearing person Current antimicrobial therapy <sup>(a)</sup> Convalescent phase of illness Preterm birth (hepatitis B vaccine is an exception in certain circumstances) <sup>(b)</sup> Recent exposure to an infectious disease History of penicillin allergy, other nonvaccine allergies, relatives with allergies, or receiving allergen extract immunotherapy History of GBS <sup>(c)</sup>
DTaP	Fever within 48 hours after vaccination with a previous dose of DTP or DTaP Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP Seizure ≤3 days after receiving a previous dose of DTP/DTaP Persistent, inconsolable crying lasting ≥3 hours within 48 hours after receiving a previous dose of DTP/DTaP Family history of seizures Family history of sudden infant death syndrome Family history of an adverse event after DTP or DTaP administration Stable neurologic conditions (e.g., cerebral palsy, well-controlled seizures, or developmental delay)
Hepatitis B	Pregnancy Autoimmune disease (e.g., systemic lupus erythematosus or rheumatoid arthritis)
HPV	Immunosuppression Previous equivocal or abnormal Papanicolaou test Known HPV infection Breastfeeding History of genital warts
ΙΙV	Nonsevere (e.g., contact) allergy to latex, thimerosal, or egg Concurrent administration of Coumadin (generic: warfarin) or aminophylline
IPV	Previous receipt of ≥1 dose of oral polio vaccine
LAIV	Health-care providers that see patients with chronic diseases or altered immunocompetence (an exception is providers for severely

MMR<sup>(d),(e)</sup>

PPSV23

Rotavirus

Tdap

Varicella

Zoster

immunocompromised patients requiring care in a protected environment) Breastfeeding Contacts of persons with chronic disease or altered immunocompetence (an exception is contacts of severely immunocompromised patients requiring care in a protected environment)

Positive tuberculin skin test Simultaneous tuberculin skin or interferon-gamma release assay (IGRA) testing<sup>(f)</sup> Breastfeeding Pregnancy of recipient's mother or other close or household contact Recipient is female of child-bearing age Immunodeficient family member or household contact Asymptomatic or mildly symptomatic HIV infection Allergy to eggs

History of invasive pneumococcal disease or pneumonia

Prematurity Immunosuppressed household contacts Pregnant household contacts

History of fever of  $\ge 40.5^{\circ}$ C ( $\ge 105^{\circ}$ F) for <48 hours after vaccination with a previous dose of DTP or DTaP

History of collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP History of seizure <3 days after receiving a previous dose of DTP/DTaP

History of persistent, inconsolable crying lasting >3 hours within 48 hours after receiving a previous dose of DTP/DTaP

History of extensive limb swelling after DTP/DTaP/Td that is not an Arthus-type reaction

History of stable neurologic disorder

History of brachial neuritis

Latex allergy that is not anaphylactic

Breastfeeding Immunosuppression

Pregnancy of recipient's mother or other close or household contact Immunodeficient family member or household contact<sup>(g)</sup> Asymptomatic or mildly symptomatic HIV infection Humoral immunodeficiency (e.g., agammaglobulinemia)

Therapy with low-dose methotrexate (<0.4 mg/kg/week), azathioprine (<3.0 mg/kg/day), or 6-mercaptopurine (<1.5 mg/kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease, or other conditions Health-care providers of patients with chronic diseases or altered immunocompetence Contacts of patients with chronic diseases or altered

immunocompetence

Unknown or uncertain history of varicella in a U.S.-born person

Abbreviations: DT = diphtheria and tetanus toxoids; DTP = diphtheria toxoid, tetanus toxoid, and pertussis; DTaP = diphtheria and tetanus toxoids and acellular pertussis; GBS = Guillain-Barré syndrome; HBsAg = hepatitis B surface antigen; Hib = Haemophilus influenzae type b; HIV = human immunodeficiency virus; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; Td = tetanus and diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

(a) Antibacterial drugs might interfere with Ty21a oral typhoid vaccine, and certain antiviral drugs might interfere with varicella-containing vaccines and LAIV4.

(b) Hepatitis B vaccination should be deferred for infants weighing <2,000 g if the mother is documented to be HBsAg negative. Vaccination should commence at chronological age 1 month or at hospital discharge. For infants born to HBsAg-positive women, hepatitis B immune globulin and hepatitis B vaccine should be administered within 12 hours after birth, regardless of weight.

<sup>(r)</sup> An exception is Guillain-Barré syndrome within 6 weeks of a dose of influenza vaccine or tetanus-toxoid-containing vaccine, which are precautions for influenza vaccines and tetanustoxoid containing vaccines, respectively.

(d) MMR and varicella vaccines can be administered on the same day. If not administered on the same day, these vaccines should be separated by at least 28 days.

(e) HIV-infected children should receive immune globulin after exposure to measles. HIV-infected children can receive varicella and measles vaccine if CD4+ T-lymphocyte count is >15%. (54).

<sup>(f)</sup> Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin or IGRA testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for at least 4 weeks after the vaccination. If an urgent need exists to skin test or IGRA, do so with the understanding that reactivity might be reduced by the vaccine.

<sup>(g)</sup> If a vaccinee experiences a presumed vaccine-related rash 7-25 days after vaccination, the person should avoid direct contact with immunocompromised persons for the duration of the rash.

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## **File Formats Help:**

How do I view different file formats (PDF, DOC, PPT, MPEG) on this site? (https://www.cdc.gov/Other/plugins/)

(https://www.cdc.gov/Other/plugins/#pdf)

Page last reviewed: January 10, 2019

Page last updated: January 10, 2019

Content source: National Center for Immunization and Respiratory Diseases (/ncird/index.html)

2/28/19, 12:29 PM Page 11 of 10 https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contr\_\_YInouUQsjSUapMsEXxtggZPeWw9\_4LJZk8sL1\_77E\_-puZpCYNvs\_\_



# **Global Measles Burden**

- Measles is still commonly transmitted (endemic or large Asia, the Pacific, and Africa outbreaks) worldwide, including some countries in Europe,
- infant mortality. Measles remains a leading cause of vaccine-preventable
- Great progress has been made towards measles elimination
- From 2000-2016\*:
- per million persons Reported measles incidence decreased 87%, from 145 to 19 cases
- deaths prevented) Annual estimated measles deaths decreased 84% (20.4 million

\*Source: MMWR: Oct 27, 2017 / Vol. 66 / No. 42



## Before 1963 Vaccine Development\* **U.S.** Measles Burden:

- Each year, measles caused an estimated 3 to 4 million cases
- Close to 500,000 cases were reported annually to CDC, resulting in:
- 48,000 hospitalizations
- 1,000 cases with encephalitis (brain swelling)
- 450 to 500 deaths

# **U.S. Measles Burden: Current\***

- Measles was declared eliminated from the United States in other control measures. 2000 thanks to a highly effective vaccination program and
- and can be brought into the United States by unvaccinated travelers (Americans or foreign visitors). However, measles remains present in many other countries
- This can result in outbreaks that are costly to control.
- ranged from 37 people in 2004 to 667 people in 2014. Since 2000, the annual number of reported measles cases
- The last measles death in the United States occurred in 2015.

\*Source: www.cdc.gov/measles

## Slide 5 Notes

absence of continuous measles transmission for greater than 12 months. Measles elimination is a global problem. Elimination means



## Slide 7 Notes

years of age and adults older than 20 years of age are more likely to suffer from Measles can be a serious in all age groups. However, children younger than 5 measles complications.

## Common Complications

- Common measles complications include ear infections and diarrhea.
- Ear infections occur in about one out of every 10 children with measles and can result in permanent hearing loss
- Diarrhea is reported in less than one out of 10 people with measles

## Severe Complications

- Some people may suffer from severe complications, such as pneumonia (infection of the lungs) and encephalitis (swelling of the brain). They may need to be hospitalized and could die.
- young children. As many as one out of every 20 children with measles gets pneumonia, the most common cause of death from measles in
- convulsions and can leave the child deaf or with intellectual disability. About one child out of every 1,000 who get measles will develop encephalitis (swelling of the brain) that can lead to
- For every 1,000 children who get measles, one or two will die from it.

## Long-term Complications

- the person seems to have fully recovered from the illness. Since measles was eliminated in 2000, SSPE is rarely reported in the measles virus infection acquired earlier in life. SSPE generally develops 7 to 10 years after a person has measles, even though Subacute sclerosing panencephalitis (SSPE) is a very rare, but fatal disease of the central nervous system that results from a United States
- measles before they are two years of age. Among people who contracted measles during the resurgence in the United States in 1989 to 1991, 4 to 11 out of every 100,000 were estimated to be at risk for developing SSPE. The risk of developing SSPE may be higher for a person who gets 00



## Slide 9 Notes

- contribute to an increase in measles cases in the U.S. An outbreak is 3 or more cases. Outbreaks in countries to which Americans often travel can directly
- Reasons for an increase in cases some years:
- the Philippines in 2014. the measles virus type in this outbreak (B3) was the same virus type that caused the large measles outbreak in the amusement park while infectious; however, no source was identified. Analysis by CDC scientists showed that 2015: The United States experienced a large, multi-state measles outbreak linked to an amusement park in California. The outbreak likely started from a traveler who became infected overseas with measles, then visited
- associated with cases brought in from the Philippines, which experienced a large measles outbreak. For more 2014: The U.S. experienced 23 measles outbreaks in 2014, including one large outbreak of 383 cases, occurring information see the Measles in the Philippines Travelers' Health Notice. primarily among unvaccinated Amish communities in Ohio. Many of the cases in the U.S. in 2014 were
- with 58 cases. For more information see Measles United States, January 1-August 24, 2013. 2013: The U.S. experienced 11 outbreaks in 2013, three of which had more than 20 cases, including an outbreak
- For more information see Measles United States, January-May 20, 2011. was experiencing a large outbreak. Most of the cases that were brought to the U.S. in 2011 came from France. 2011: In 2011, more than 30 countries in the WHO European Region reported an increase in measles, and France
- see Update: Measles United States, January-July 2008. people. The U.S. experienced several outbreaks in 2008 including three large outbreaks. For more information 2008: The increase in cases in 2008 was the result of spread in communities with groups of unvaccinated

# Measles in the United States, 2016\*

- 86 cases reported from 19 states; 4 outbreaks
- 97% cases import-associated
- Of the 18 direct importations, 12 were U.S. residents, 6 were foreign visitors
- 73% were outbreak-related
- Outbreaks ranged in size from 6 to 32 cases
- Cases among U.S. residents (N=55)
- 56% unvaccinated
- 18% unknown vaccination status
- 26% vaccinated

**U.S. Economic Burden of Measles\*** 

\$142,000	1	lowa	2004
\$168,000	34 (1)	Indiana	2005
\$800,000 (limited to cost for 2 hospitals to respond to 7 cases in their facilities)	14 (1)	Arizona	2008
\$125,000	12 (1)	California	2008
>\$330,000	13 (2)	Utah	2011
\$2.7-5.3 million	107 (16)	SN	2011
Estimated public health cost^	Number of cases (outbreaks)	Location	Vear

\*Sources www.ncbi.nlm.nih.gov/pubmed/24135574, www.nejm.org/doi/full/10.1056/NEJMoa060775, ^Public health and health care costs expended to control the spread of measles http://pediatrics.aappublications.org/content/116/1/e1 http://pediatrics.aappublications.org/content/125/4/747, http://jid.oxfordjournals.org/content/early/2011/04/25/infdis.jir115.full

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## Slide 12 Notes

A 2008 outbreak in 2 Arizona hospitals with 7 health-care associated infections:

- No electronic vaccination records for healthcare personnel
- ${\sim}15,000$  hrs were lost in furloughs (because of exposure, disease, or lack of evidence of immunity)
- Cost the facilities \$800,000 to respond to 7 cases (e.g., vaccination costs, record reviews, furloughs)
- providing vaccinations for healthcare workers. The costs related to the AZ outbreak included obtaining evidence of immunity for healthcare workers and
- Measles is due to failure to vaccinate. Case investigations are very resource-intensive.
- lose sight of the many successes that have been achieved. Luckily we have safe and effective vaccines that can prevent much of this burden, and we should not
- estimated 322 million illnesses, 21 million hospitalizations, and 732,000 deaths over the course of Modeling estimated that, among children born during 1994–2013, vaccination will prevent an their lifetimes, at a net savings of \$295 billion in direct costs and \$1.38 trillion in total societal costs.
- Additional successes include the fact that outbreaks since measles elimination have generally been limited (in both size & number of generations)
- We have maintained high overall vaccine coverage.
- We have a very rapid/aggressive public health response to suspect cases.
- Elimination has been achieved & maintained for 15 years.
- achievable The vaccine works and the disease is recognizable which makes eradication both possible & 13

# Measles Resources from CDC

## General information

- Measles website: www.cdc.gov/measles
- Measles resources: http://www.cdc.gov/measles/resources/
- Feature on measles: <a href="http://www.cdc.gov/features/measles/">www.cdc.gov/features/measles/</a>
- Measles vaccination website:
- www.cdc.gov/measles/vaccination.html
- Vaccine schedules: <a href="http://www.cdc.gov/vaccines/schedules/index.html">www.cdc.gov/vaccines/schedules/index.html</a>
- For Healthcare Professionals: <u>www.cdc.gov/measles/hcp/index.html</u>
- Surveillance Manual: <a href="http://www.cdc.gov/vaccines/pubs/surv-">www.cdc.gov/vaccines/pubs/surv-</a> manual/chpt07-measles.html

## Materials for travelers

 Traveler's health measles page: wwwnc.cdc.gov/travel/diseases/measles



When measles happens anywhere in the world...

recommended doses of MMR for best protection against measles measles-mumps-rubella (MMR) vaccine, including before traveling internationally. Ask your doctor if everyone has received all Make sure you and your family members are up-to-date on your Since measles is still common in many countries, unvaccinated travelers will www.cdc.gov/features/measles/ CDC U.S. Department of Health and Human Ser

For more information please contact the Centers for Disease Control and Prevention

Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348 1600 Clifton Road NE, Atlanta, GA 30333

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



## Adversomics: a new paradigm for vaccine safety and design

Jennifer A. Whitaker, MD, MSc, Inna G. Ovsyannikova, PhD, and Gregory A. Poland, MD

## Summary

Despite the enormous population benefits of routine vaccination, vaccine adverse events and reactions, whether real or perceived, have posed one of the greatest barriers to vaccine acceptance—and thus to infectious disease prevention—worldwide. A truly integrated clinical, translational, and basic science approach is required to understand the mechanisms behind vaccine adverse events, predict them, and then apply this knowledge to new vaccine design approaches that decrease, or avoid, these events. The term "adversomics" was first introduced in 2009 and refers to the study of vaccine adverse reactions using immunogenomics and systems biology approaches. In this review, we present the current state of adversomics research, review known associations and mechanisms of vaccine adverse events/reactions, and outline a plan for the further development of this emerging research field.

Keywords: Vaccines, Viral Vaccines, Immunogenetics, Genetic Association Studies, Systems Biology, Individualized Medicine, Vaccination, Genomics, Drug-Related Side Effects and Adverse Reactions, Polymorphism, Single Nucleotide

## Vaccine Adverse Events and Reactions

The use of vaccines to prevent communicable diseases is among the greatest public health achievements of the 20<sup>th</sup> century [1]. However, despite technologic advances in developing newer and more efficacious vaccines, systems-level improvements in national immunization programs, and the expansion of these programs to remote corners of the developing world, scientists and healthcare workers worldwide continue to fight the age-old foe of vaccines, namely, fear [2–9]. This fear ranges from logical concern and illogical anxieties regarding known vaccine adverse reactions to panic over unproven and imagined sequelae of vaccination [2,4,10–13]. In one case-control study of parental vaccine refusal in the United States, the most common reason for vaccine refusal was fear that the vaccine itself might cause harm (57%) [12].

Prophylactic vaccines are held to greater safety standards than many other drugs and biologic products, principally because they are given to largely healthy populations with the intent to prevent, rather than treat, disease. Vaccines are designed to stimulate an immune response to an antigen, and, in so doing, they often produce inflammatory effects. Usually, these reactions are mild and manifest as mild local or systemic adverse reactions to a vaccine such as redness, swelling, or fever. Uncommonly, the immune response may result in a more severe or prolonged adverse reaction. Rarely, a life-threatening allergic reaction may occur after vaccination. Specific diagnostic criteria for establishing a case of anaphylaxis after immunization have been established [14]. A vaccine adverse reaction is defined by the U.S. Centers for Disease Control and Prevention (CDC) as "an untoward effect caused by a vaccine that is extraneous to the vaccine's primary purpose of producing immunity" [15]. Vaccine adverse reactions are often termed vaccine side effects. The term "vaccine adverse event" refers to any untoward medical event that occurs following vaccination [15]. An adverse event may be a true adverse reaction that is caused by the vaccine or an unrelated, coincidental event. Investigation is required to determine if the adverse event is caused by the vaccine. The World Health Organization (WHO) has published a manual for causality assessment of adverse events following immunization (AEFI) [16,17]. It is important to perform a systematic evaluation of all possible causes of an AEFI that includes assessment of the temporal relationship, biological plausibility, consideration of alternative explanations (e.g., pre-existing illness, onset of new illness that is not related to immunization, spontaneous occurrence of an event without known risk factors, onset of a genetically programmed disease, recent exposure to another infectious agent or toxin prior to the event, occurrence of the event in the past independent of immunization, possible medication effects), and prior evidence that the vaccine has been shown to cause the particular event [16]. The WHO causality assessment involves a fourstep process of assessing eligibility of an event as an AEFI that results in classification of the event as "consistent causal association to immunization," "indeterminate," "inconsistent causal association to immunization" (coincidental), or "unclassifiable" (Table 1) [16]. The association is "indeterminate" when adequate information on the AEFI is

available, but it is not possible to assign it to "consistent causal association" or "inconsistent causal association to immunization." An event is "unclassifiable" when additional information is required to determine causality [16]. Vaccine-product reactions may be related to the vaccine antigen(s), another vaccine component, and adjuvant (if present), or a combination of the vaccine antigen(s) and adjuvant. The frequency of vaccine adverse reactions vary by vaccine type and characteristics of the patient population examined. Vaccines may unmask susceptibility toward a vaccine adverse event in certain populations (e.g., fever after vaccination may result in febrile seizures in children with a predisposition for seizure disorders). Vaccine immunogenicity is influenced by multiple individual patient factors (e.g., age, sex, comorbidities, genetics) and vaccine factors (e.g., antigen dose, vaccine delivery mechanism, vaccine schedule, and vaccine adjuvant). These factors may also influence inflammatory responses, which may in turn lead to vaccine adverse effects. WHO classifies vaccine product-related and vaccine quality defect-related reactions as those "associated with route or site of administration," "immune-mediated," and "reactions as a consequence of replication of a vaccine associated microbial agent" (Table 1). "Reactions as a consequence of replication of a vaccine associated microbial agent" are more likely to occur in patients who are immunosuppressed. The mechanisms behind these adverse reactions to live vaccines are different than immune-mediated reactions to inactivated vaccines.

> Table 1 WHO Classification of Adverse Events Following Immunization,

Immune-mediated vaccine adverse events that have been found to have a causal association with a vaccine are ideal targets of study for the field of adversomics. Compared to the significant focus on vaccine immunogenicity, less attention has been paid to factors that influence immune-mediated adverse vaccine events and the mechanisms behind these events. Understanding and preventing serious adverse vaccine events is critical to improving public trust in vaccine safety and to developing new safe and effective vaccines. In this regard, much can be gleaned from the fields of personalized medicine and pharmacogenomics to offer a new paradigm for understanding and predicting adverse vaccine events. In turn, these observations may then aid in the design of new vaccines that avoid or decrease the frequency of these vaccine adverse events.

## Personalized Medicine, Vaccinomics, and Adversomics

The principles of "personalized medicine" apply equally to "personalized vaccinology"—by which we mean that the choice of the vaccine administered should take into account critical characteristics of the individual. We could administer the right vaccine, at the right dose, for the right patient, at the right time. Not all individuals respond in the same way to vaccines. There is an optimal personalized vaccine approach, consisting of an optimal vaccine formulation, route of administration, adjuvant, dose, and dosing schedule (for vaccines that require multiple doses) for an individual or group of individuals. We have called for the application of "vaccinomics" to help us understand the genetic and non-genetic factors influencing the immune response to a vaccine antigen at the systems level [18–24]. Similarly, we have called for the development of "adversomics"—the application of immunogenomics and systems biology to understand the genetic and non-genetic drivers of vaccine adverse reactions at the molecular level [18,25,26].

The field of pharmacogenomics has demonstrated that exploratory genomics discovery studies can lead to validated biomarkers that can be used to predict risk for adverse drug reactions. One elegant example is the link between the human leukocyte antigen (HLA) HLA\*B57:01 and potentially fatal idiosyncratic hypersensitivity to the HIV medication abacavir. Prior to using genetic testing, hypersensitivity reactions occurred in 5–8% of patients within the first six weeks of starting abacavir therapy [27].Shortly after abacavir approval in the United States, an association between abacavir hypersensitivity and HLA-B\*57:01 was published, [28,29],replicated, and validated across multiple patient cohorts [30,31]. Further research demonstrated that the precise mechanism by which abacavir . binds non-covalently to the peptide binding groove floor of HLA-B\*57:01 and alters the presentation of self-peptides presented to the immune system and activation of CD8+ T-lymphocytes, which results in the release of inflammatory

cytokines that cause the clinical hypersensitivity reaction [32–35]. This specificity explains the 100% negative predictive value of HLA-B\*57:01 genetic testing for abacavir hypersensitivity [31], which has resulted in its widespread use and incorporation into U.S. HIV treatment guidelines [36,37]. Other examples of hypersensitivity reactions to particular drugs and specific HLA associations include allopurinol (HLA-B\*58:01) and carbamazepine (HLA-B\*15:02) [38]. The field of pharmacogenomics is rapidly evolving with further applications of genetic variations beyond idiosyncratic drug reactions to effects on pharmacokinetics, pharmacodynamics, and molecular defects related to the pathogenesis of certain malignancies for which specific targeted treatments have been developed. At this time, no such elegant examples exist for explanations or mechanisms of immunologically medicated vaccine adverse reactions, emphasizing the need for additional research in this field.

## Adversomics-Current State of the Field

The field of vaccine adversomics, as we have described it [39], is really an extension of pharmacogenomics. However, when compared to the field of pharmacogenomics (which studies drugs), the field of vaccine adversomics is in its infancy. At this time, these technologies are not being used clinically. The first step in advancing this science is to use adversomics research techniques to understand the mechanisms behind adverse events that have a causal relationship with immunization. We propose that the same methodologies that have been used to study drugs can and should be applied to the study of vaccines. The precise mechanisms of adverse reactions associated with vaccines are not well understood. Understanding the molecular/genetics/proteomics level (i.e., adversomics) involvement, specifically how genetics (genomics and transcriptomics) impact the development of vaccine adverse reactions, may aid in the design of newer and safer vaccine candidates [25,39]. Table 2 provides a comprehensive review of what has been published in the field of adversomics to date.



## Evaluating Causation of Alleged Vaccine Adverse Events—Childhood Immunizations and Seizure Disorders

One important lesson that can be learned from the application of genomics to the study of vaccine adverse events (AEs) is that not all AEs are actually related to the vaccine. A recent study by Verbeek and colleagues demonstrated that, in most cases, genetic or structural defects are the underlying cause of epilepsy onset after routine immunization in children [40]. They examined data for 990 children who experienced seizures following immunization (four doses of DTaP, a dose of MMR and Haemophilus influenza type B vaccines) during the first two years of life. Of the 1,022 potential epileptic seizures amongst these 990 children, 68% and 32% occurred after receiving of an inactivated vaccine and live attenuated vaccine, respectively [40]. Following DNA sequencing in 14 (61%) out of 23 children with epilepsy and vaccine-related seizure onset, underlying genetic or structural causes were identified in 15 (65%) of those children. Eleven children had Dravet syndrome associated with the SCN1A (sodium channel, voltage-gated, type I, alpha subunit) gene mutation. It was stated that "these underlying causes were not limited to SCN1A-related Dravet syndrome but extended to other genetically determined fever-sensitive epilepsies" and that "early genetic testing should be considered in all children with vaccination-related onset of epilepsy" [40]. Another study evaluated 14 patients with alleged vaccine-related seizures or seizure disorders in whom the first seizure occurred within 72 hours of vaccination after administration of trivalent diptheria-pertussis-tetanus vaccine or pentavalent diphtheria-pertussis-tetanus-inactivated polio-Haemophilus influenzae type B vaccine. These patients had genetic studies performed that resulted in diagnoses of specific epilepsy syndromes in all 14 cases [41]. These studies provide examples of how genetic testing into the cause of alleged vaccine-related AEs can be important in determining if the adverse event was coincidental or truly related to the vaccine. Such investigations are important for evaluating vaccine safety and also maintaining public trust in vaccine safety.

## Adversomics and Smallpox Vaccine

Smallpox remains a bioterrorism concern. Despite smallpox disease eradication in 1980, smallpox vaccination with the vaccinia vaccine is still being administered to some first responders, laboratory researchers, healthcare workers, and military personnel; and AEs from vaccinia virus immunization are still observed. In 2003, the U.S. Department of Health and Human Services employed a smallpox vaccination program that included a comprehensive safety monitoring system among HCWs and first responders. Over 38,000 doses of vaccine were administered and 822 AEs were reported; 100 of these AEs were considered serious [42]. AEs included: myocarditis and/or pericarditis in 21 cases, unexpected ischemic cardiac events in 10 cases, generalized vaccinia in two cases, and one case of postvaccinial encephalitis [42,43]. The smallpox vaccine is contraindicated in persons with eczema and exfoliative skin conditions due to the risk of developing vaccinia eczema vaccinatum, in which case the virus disseminates to cause an extensive vesiculopustular rash with systemic illness. The Centers for Disease Control and Prevention (CDC) recommended that those with underlying heart disease and three or more cardiac risk factors should not be vaccinated. It is important to comprehend the underlying mechanisms of these vaccine AEs so they could be better understood and perhaps predicted, and so large populations would not need to be excluded from vaccination should an event occur that would necessitate mass-vaccination. Furthermore, if these mechanisms were elucidated, this knowledge may enable the development and use of new vaccines—an advancement that may result in avoiding these events altogether.

Several recent studies, as reviewed below, have addressed the association between gene polymorphisms and predisposition for AEs after smallpox vaccination. The first example is a study of local and systemic AEs (i.e., fever, generalized skin eruptions, and lymphadenopathy) following smallpox vaccine [44]. Reif *et al.* conducted two studies of healthy vaccinia-naïve adults (n=85 and n=46 subjects, respectively), who received the Aventis Pasteur smallpox vaccine (APSV) and were evaluated at fixed time points (days 3–5, 6–8, 9–11, 12–15, and 26–30) after vaccine. In the first study of 85 subjects, 16 had systemic AEs; in the second study of 46 subjects, 24 subjects had systemic AEs. All subjects were genotyped for 1,442 SNPs that originated from 386 candidate genes. The investigators found specific SNPs/haplotypes in the *MTHFR* (enzyme 5,10-methylenetetrahydrofolate reductase, non-synonymous rs1801133, p<0.01) and *IRF1* (interferon regulatory factor-1, rs9282763 and synonymous rs839, p=0.03) genes that were significantly associated with AEs in both studies [44]. Genetic variants in the *MTHFR* gene have been previously associated with adverse reactions to other pharmacologic biologics [45,46]. As the authors wrote, protein products of the *MTHFR* and *IRF1* genes may play an important role in homocysteine metabolism, as well as roles in regulating endothelial function and activating transcription of the Type I ( $\alpha$  and  $\beta$ ) and Type II ( $\gamma$ ) interferons, respectively.

Cases of myocarditis and myopericarditis after smallpox vaccination have been reported. Smallpox vaccine studies, including studies examining genetic predisposition for AEs after smallpox vaccine, have been conducted in order to examine the mechanisms behind these vaccine adverse events [47–52]. Variola virus, the causative agent of smallpox, does not directly cause cardiovascular complications, but vaccinia virus vaccine (Dryvax, ACAM2000) has been associated with electrocardiogram (ECG) and cardiac enzyme abnormalities and occasionally with signs and symptoms associated with myocarditis and myopericarditis [42,48,49]. It is not understood whether vaccinia-associated myopericarditis is due to direct viral injury, secondary to the immune response, host genetics or a combination of these and other factors in the studied populations. A better understanding of the genetic and immunologic factors related to vaccinia-associated myopericarditis is needed, and such studies are currently being conducted in our laboratory.

The genetic basis for developing fever (defined as a temperature >37.7°C) after smallpox (Dryvax) vaccination has been evaluated [53]. A total of 357 SNPs in 19 immune-related genes were examined for each of the 346 healthy study subjects after vaccination with live vaccinia virus vaccine. This study found that specific haplotypes in the *IL1* and *IL18* genes are associated with the development of fever and differences in humoral immunity after smallpox vaccine. The exact mechanisms are not known, but in a mouse model of coxsackie virus-induced myopericarditis, elevated levels of IL-1 and IL-18 cytokines have been related to myocardial inflammation, and inhibition of IL-1 action (using IL-1 receptor antagonist) improved both inflammation and mortality [53,54]. In addition, this study identified a haplotype in the *IL4* gene that was highly significant for its association with decreased likelihood of fever after vaccine in vaccine naïve subjects. This *IL4* haplotype includes the SNP rs2243250 that is

associated with augmented secretion of an important Th2 regulatory cytokine, IL-4, known to inhibit IFN- $\gamma$  production and Th1 response [55,56]. In a study of 580 healthy Caucasian individuals (19–40 years old) after a single dose of Dryvax vaccine, genetic variation in the *IL1R, IL18*, and *IL18R1* genes was linked to vaccinia-specific IL-1 $\beta$  production [57]. We believe that functional studies of genetic variants are needed to gain knowledge into the mechanisms by which these SNPs/haplotypes contribute to smallpox vaccine immunity and vaccine-associated AEs. The potential involvement of *IL1, IL18, IL4* and other genes in AEs associated with the administration of other vaccines (e.g., MMR, MMRV, yellow fever, hepatitis B, influenza, anthrax, etc.) is of great interest and should also be further investigated.

## Adversomics and Yellow Fever Vaccine

The live attenuated yellow fever vaccine 17D (YF-17D) is a well-tolerated vaccine with very few known cases of vaccineassociated AEs. However, there is a rare, but serious, risk of severe yellow fever-like disease due to the vaccine strain of the virus. Yellow fever vaccine 17D–induced viscerotropic disease is a serious vaccine AE characterized by multiple- organ system failure that has a high fatality rate [58,59]. It has been suggested that yellow fever vaccine-associated viscerotropic disease is associated with persistent viremia, robust induction of T and B cell responses, and polymorphisms in the chemokine receptor *CCR5* (delta 32) and its ligand *RANTES* (403G/A) genes [58]. Further, Bae *et al.* noted that serum cytokines and chemokines, such as RANTES, IL-6, IL-8, MIG (monokine induced by IFN- $\gamma$ ), GRO (growth-related oncogene), MCP-1 (monocyte chemotactic protein), TGF- $\beta$ (transforming growth factor), and TNF- $\beta$  (tumor necrosis factor) may be considered as surrogate markers for individuals likely to develop severe yellow fever-associated AEs, such as vaccine-associated neurotropic and viscerotropic diseases [60]. It is possible that increased and/or decreased production of these biological markers, due to polymorphisms in these genes, may have impaired the immune response to YF vaccine. On the other hand, Martins *et al.* studied 50 subjects vaccinated with 17DD YF vaccina and CD8+HLA-DR+ lymphocytes at day 30 post-vaccination may be reliable markers for an immune response that is free of AEs after YF vaccination [61]. These studies provide initial insights into yellow fever vaccine AEs; however, we are a long way from understanding the mechanisms behind these AEs or being able to predict them.

## Adversomics and Influenza Vaccine

## Guillain-Barré Syndrome

Although the risk of Guillain-Barré syndrome (GBS) following influenza vaccination has been shown to be lower than after influenza illness [62], there is still significant public concern regarding vaccination leading to this neurologic condition. Immune response to microbial antigens that are cross-reactive with neural epitopes may trigger an inflammatory disorder – GBS--in which genetic host factors may impact disease susceptibility. In 1976–1977, there was an increased risk of GBS following vaccination with the swine influenza vaccine, with an estimated attributable risk of GBS after vaccine in adults of just under 1 case per 100,000 vaccinations and a relative incidence (RI) of 7.6 (95% CI, 6.7–8.6) [63,64]. The precise reason for this relationship is not known. Recently, the effects of gene polymorphisms on GBS risk have been recognized for several genes: TNF- $\alpha$  (tumor necrosis factoralpha) gene (polymorphisms 308 G/A and 857 C/T), *TLR4* (toll-like receptor 4) gene (Asp299Gly and Thr399Ile), *FcRL3* (Fc receptor like 3) gene (FcRL3-3–169C, FcRL3–6 intron3A, and FcRL3–8 exon15A), and *MMP9* (matrix metalloproteinase 9) gene (C-1562T) [65–68]. However, these studies examined populations with GBS without examining potential inciting causes, such as recent infections or receipt of other vaccines. It is difficult to know if these polymorphisms should be explored in relationship to GBS that has occurred after vaccination.

## Narcolepsy

After the 2009–10 influenza A H1N1 pandemic and large vaccination campaigns with the AS03-adjuvanted influenza A H1N1 Pandemrix vaccine in Europe, an increase in the incidence of narcolepsy was reported in Sweden and Finland [69–71]. Narcolepsy

is believed to be an autoimmune disease that is caused by the loss of hypothalamic hypocretin-producing neurons [72]. It has been found to have a strong association with the HLA-DQB\*06:02 allele in people of all ethnicities. Using strict diagnostic criteria, 98% of patients with narcolepsy and cataplexy are DQB1\*06:02 positive [73,74]. It is important to note that in another case-control study of narcolepsy after AS03-adjuvanted influenza A II1N1 vaccination, the HLA-DQB\*06:02 allele was found in 100% of narcolepsy cases (47/47), but also in 35% (20/57) of controls [75]. The presence of this allele may be necessary, but not sufficient to result in the vaccine adverse event. The HLA-DQB1\*06:02 allele is present in 13-28% of Caucasian populations; however, the risk of narcolepsy in children vaccinated with Pandemrix who carry this allele is only 1 in 1,600 [76]. It has been hypothesized that the AS03-adjuvanted A/H1N1 vaccine resulted in molecular mimicry with a neuronal autoantigen. One study that provided further support for this hypothesis was later retracted due to an inability to replicate the data [77]. Questions remain as to why one AS03 adjuvanted A/H1N1 (Pandemrix) vaccine seems to have led to an increase in narcolepsy cases, while another AS03 adjuvanted A/H1N1 vaccine (Arepanrix), which was prepared by a slightly different inactivation protocol did not [78]. Further work demonstrated that antibody to Pandemrix-derived nucleoprotein (NP) was increased in patients with narcolepsy and the DQB1\*06:02 risk allele of narcolepsy appeared to regulate the anti-NP immune response [75]. The authors of this study hypothesized that the differences in the H1N1 antigens of Arepanrix and Pandemrix could explain the differences in vaccineattributable risk of narcolepsy between these vaccines and call for the screening of NP derived DQB1\*06:02 dependent epitopes [75].

## Understanding HLA Gene Effects

The field of adversomics would further benefit from an understanding of HLA gene contributions to vaccine-induced immune responses, including AEs. For example, recombinant hepatitis B vaccine-associated major AEs have been hypothesized as being linked to HLA class II DRB1 alleles/haplotypes (\*01:01, \*03:01, \*04:01,\*13:01, \*15:01) and HLA class I A2 gene interaction [79]. The authors speculate that the presence of the specific HLA allele can result in activation of cytotoxic CD8+ T cells by HLA-A2 presented hepatitis B surface antigens (HBsAg), causing production of high levels of IFN- $\gamma$ , TNF, and augmentation of vaccine AEs. In fact, several HLA class II DRB1 alleles/haplotypes are linked to hepatitis B vaccine non-response [80,81]. HLA polymorphisms have also been shown to be related to non- and low-response to measles, mumps, rubella, and anthrax vaccines [82–87]. It has been proposed that susceptibility-related HLA class I and class II alleles may drive the development of vaccine AEs after hepatitis B vaccination [79].

The application of genotype-phenotype knowledge will be critical to developing models of genetic predisposition to vaccine adverse effects. Lin et al. have created an Ontology of Genetic Susceptibility Factors (OGSF) which may provide a framework for genetic susceptibility to vaccine-associated AEs [88]. The OGSF uses genetic studies and accounts for diverse types of genetic susceptibility factors, such as HLA alleles, SNPs, genes, and gene haplotypes, and may be useful for identification of true genetic factors/determinants contributing to the susceptibility to vaccine AEs.

## Adversomics Research Challenges

There are multiple challenges in adversomics research. First, as depicted in the aforementioned examples, many vaccine AEs are quite rare. This low frequency makes them difficult to identify and to study. Unlike the case of abacavir hypersensitivity, which occurred in 5–8% of persons treated with the medication, many events occur at the level of a few cases per 100,000 population (i.e., GBS), and some occur at even lower frequency (i.e., YF vaccine-associated neurotropic or viscerotropic disease). Second, it is often difficult to prove causality for a vaccine adverse event. Some conditions or symptoms that have been attributed to vaccines are coincidental and not causal. Reported symptoms that are unrelated to the vaccine (such as in the cases of genetically predetermined epilepsy) can cause confounding of analyses. The difficulty in determining causality makes it difficult to identify which outcomes are truly the ones that need to be investigated. Third, in some countries (for example, in the U.S), the system for reporting vaccine AEs is passive. In the U.S., vaccine adverse events are reported to the Vaccine Adverse Event Reporting System (VAERS), which is a CDC- and Food and Drug Administration (FDA)-sponsored post-marketing vaccine adverse events surveillance system. Many vaccine AEs may never be reported, which limits our ability to identify and study these events. Some
other countries have active vaccine adverse events surveillance systems. Fourth, there is no efficient system by which we can obtain samples from persons with proven vaccine AEs. Biobanks have been created for multiple disease conditions, but such repositories do not currently exist for vaccine AEs.

## Adversomics and Vaccine Design

We recognize the limitations and challenges with adversomics research. At this point in time, the field is in its infancy. It is currently not practical or cost-effective to perform genotyping on a patient and then select a particular vaccine based on these genomic results. Furthermore, in some cases, as in the example of narcolepsy and Pandemrix, the frequency of the allele associated with the vaccine adverse event may be very common in the population, but only a small percentage of persons with this HLA-type may experience the vaccine adverse event. We are not advocating screening populations for particular HLA types and then withholding vaccination in these persons at this time. Vaccination is important for individuals, but it is also important for the "herd." While we note that personalized medicine may help us understand and predict who is at risk for vaccine adverse events, we suggest using this science to develop vaccines that are safer for the greater population and can be used to design vaccines that will increase "herd immunity." It would be more efficient and cost-effective to use adversomics research to elucidate the mechanisms underpinning vaccine AEs and use this understanding to design or "reverse-engineer" new vaccines that minimize or avoid these events. Initial observations from the adversomics studies that we have reviewed suggest that persons with particular HLA types may have increased rates of vaccine adverse events. As has been suggested in the case of Pandemrix vaccination and narcolepsy, there may be particular vaccine epitopes that bind particular HLA molecules and trigger a more exuberant inflammatory response, resulting in increased local and systemic adverse reactions, or recognize "self," resulting in idiosyncratic adverse reactions. Particular vaccine epitopes may skew the immune response in such a manner that is harmful, rather than helpful. As the fields of structural biology and peptide-based vaccine research advance, we anticipate that not only will promiscuous peptides that induce optimal immunogenicity across HLA types be selected, but also those that do not recognize "self" and result in immunologically mediated vaccine adverse events. In the case of narcolepsy and Pandemrix, if particular vaccine NP derived DQB1\*0:02 epitopes are identified and found to be associated with narcolepsy, then, in the future, rational vaccine design could result in vaccines that avoid the presentation of these epitopes altogether.

Adversomics research extends beyond personalized vaccinology or understanding adverse reactions in only some groups of those vaccinated. Consider the example of vaccines for RSV infection. In the 1960s, a candidate formaldehye-inactivated RSV vaccine was found to enhance RSV infection in some children who experienced infection with wild-type RSV after immunization with this candidate RSV vaccine [89]. Subsequent studies in animal models have suggested that the vaccine-enhanced infection may have been associated with the generation of low-avidity antibodies [90] and an imbalanced  $T_{H2}$  response [91,92]. The studies of these adverse vaccine outcomes have informed the structure-based design of new RSV vaccine candidates [93,94].

Some of the known vaccine adverse reactions are lacking from Table 2. For example, consider the association between the rotavirus vaccine Rotashield and intussusception. If the mechanism behind this association had been elucidated, or if those who were at risk for developing intussusception might have been predicted, the story of rotavirus vaccines may have been different. Perhaps it could have led to the development of new vaccines that would have avoided this adverse event altogether [95]; however, these mechanisms have not been elucidated. New rotavirus vaccines have been created, and although the frequency of intussusception is lower than with Rotashield, and the benefits of vaccination far outweigh the very low risk of intussusception that may occur after vaccination, concern still remains for intussusception after rotavirus vaccination [96–98].

## The Role of Gender in Vaccine Adverse Events

Vaccine adverse reactions have been reported at greater rates among females for influenza [99–101], measles-mumps-rubella (MMR) [102–105], YF[106] and anthrax vaccines [107]. Females have also demonstrated superior vaccine immunogenicity to multiple vaccines [108], including influenza [99–101], measles [109], mumps [84], rubella [110], hepatitis A [111,112], hepatitis B [112,113], and smallpox [114,115]. The mechanisms behind the more vigorous immune responses noted in females merits further

exploration [26] and may provide clues to both increased vaccine AEs and increased vaccine immunogenicity in this sex. It has been proposed that sex-based differences among vaccine responses are not solely based on sex hormones, since these differences have been noted throughout all stages of life—prior to, during, and after reproductive capacity [26,108]. The effect of genetic differences between sexes, and the role these differences play in differential immune responses to vaccines, has not been fully elucidated and warrants further investigation. It might also be that females respond more vigorously to certain vaccines and require lower doses than their male counterparts. A pertinent example of an observational clinical study with varying methodologies that provides fodder for further studies is the CDC anthrax vaccine adsorbed (AVA) human clinical trial. [107]. Analysis of data from this trial demonstrated that female and Caucasian participants had a higher proportion of AVA AEs, as well as higher vaccine immunogenicity (i.e., anti-protective antigen IgG titers) [92].

## The Role of Age in Vaccine Adverse Events

Limited data exist on vaccine safety and AEs in aging population, as signs of immunosenescence are observed in this age group [101,116,117]. A review of VAERS data from 2003–2013 did not find any safety concerns for MMR vaccine in adults 19 years old and older [118]. However, in contrast to other vaccines, the YF-17D vaccine may be more frequently associated with viscerotropic AEs in older individuals [58]. The rate of YF vaccine-associated systemic AEs in individuals aged 65 or older was 2.5 times higher than the rate of AEs occurring in younger individuals (25–44 years old) [119]. With regard to influenza vaccine, systemic symptoms among older individuals ( $\geq$  65 years old) were more frequent following vaccination with high-dose (HD) trivalent, inactivated influenza vaccine (180 mcg of HA antigen) compared with a standard dose of 45 mcg [120]. It is possible that adversomic profiles may change with age.

## The Rise of Adjuvants

There has been particular concern among some groups regarding adjuvanted vaccines and their potential to cause vaccine adverse reactions. Vaccine adjuvants have been purported to cause or worsen various autoimmune inflammatory conditions. The U.S. has lagged behind many other countries in the approval of various adjuvanted vaccines. As more adjuvanted vaccines enter the markets worldwide, particular attention must be paid to whether they are associated with vaccine adverse events. If vaccine adverse events are noted, then further studies will need to be conducted to determine whether the adverse event is related to the adjuvant, to the antigens in the vaccine, or to an adjuvant-antigen combination.

## International Collaboration

International partnerships between clinicians, public health officials, epidemiologists, and clinical, translational, and basic science researchers are needed to advance the field of adversomics. In order to overcome some of the current challenges to the field, we propose the creation of a unifying infrastructure that will monitor vaccine AEs, solicit biospecimens from patients who experience these AEs, and maintain a "biobank" of these specimens for research. There are multiple agencies in the U.S. that are studying and monitoring vaccine AEs and safety, including the CDC, Vaccine Analytic Unit with Department of Defense (DOD), The FDA's Center for Biologics Evaluation and Research (CBER), the Military Vaccine Agency (MILVAX) within DOD, and individual manufacturers [25]. We propose a broader, coordinated, and more cohesive infrastructure. The oversight of all of these efforts must be coordinated and infrastructure for such an effort must be built, but we cannot stop here.

As we are reminded daily, particularly with transmission of infections across countries and continents, we live in a global community. In order to determine the rates, associations, causality, and mechanisms behind vaccine AEs, particularly the rare ones, we need an international effort of regulatory, clinical, and scientific teams working together to demystify such events. The Brighton Network [121] and WHO Global Vaccine Safety Initiative [122] are examples of collaborative international networks focused on vaccine safety research. Such international collaborative networks could be platforms for adversomics research. Through combining the spectrum of clinical, translational, and basic science research across the globe toward the goal of advancing adversomics, new knowledge will be uncovered that may identify individual risk factors, enlarge our understanding of

immune mechanisms, and define biomarkers of risk and immunity that can assist in optimizing the development of new vaccines, diagnostic tests, and therapeutics to protect humans from infectious diseases.

## Expert Commentary and Five-Year View

Future directions for adversomic research include understanding the role of female biologic sex in vaccine AEs, as females frequently have higher rates of vaccine AEs, evaluation of age and immunosenesce as a risk factor for vaccine AEs, careful attention to the role of adjuvants, and development of international collaborations and biobanks for this research.

Moreover, the promise of adversomics is to understand the mechanisms behind vaccine adverse events in order to improve vaccine safety and to personalize our approach—offering the right vaccine, at the right dose, at the right time, to the right person. Such an approach offers both safety and economic benefits. Such mechanistic information may also inform new vaccine discovery efforts.

Over the next five years, for adversomics research to move from its infancy, researchers from across the translational science spectrum need to partner together; vaccine AEs with causal associations to current licensed vaccines must be identified and thoroughly investigated; international biobanks of samples from those with vaccine-related AEs needs to be created; and immunogenetic and systems biology studies need to be conducted utilizing these samples. OMICS technologies will continue to adapt and advance. Our thinking and research methods will need to do so, as well, if we aspire to rationally design vaccines that will maximize immunogenicity and effectiveness, while minimizing adverse events.

## Key Issues

- Adversomics is the application of immunogenomics and systems biology approaches to understand the genetic and non-genetic drivers of vaccine adverse reactions at the molecular level.
- Understanding and preventing serious adverse vaccine reactions is critical to improving public trust in vaccine safety and to developing new safe and effective vaccines.
- Vaccine immunogenicity and vaccine adverse events have been reported at higher rates for females than males for multiple vaccines; This observation warrants further evaluation.
- International partnerships between clinicians, public health officials, epidemiologists, and clinical, translational, and basic science researchers are needed to advance the field of adversomics.
- An international biobank of specimens from patients with vaccine adverse events needs to be created in order to conduct further adversomics studies.

## Acknowledgments

The authors were supported by the National Institute of Allergy And Infectious Diseases of the National Institutes of Health under award numbers U01AI089859, N01AI40065, R37AI048793, and R01AI033144. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. GA Poland is the chair of a Safety Evaluation Committee for novel investigational vaccine trials being conducted by Merck Research Laboratories. GA Poland offers consultative advice on vaccine development to Merck & Co. Inc., CSL Biotherapies, Avianax, Sanofi Pasteur, Dynavax, Novartis Vaccines and Therapeutics, PAXVAX Inc, Emergent Biosolutions, Adjuvance, and Vaxness. GA Poland and IG Ovsyannikova hold two patents related to vaccinia and measles peptide research. JA Whitaker receives funding for Mayo Clinic research from Pfizer Independent Grants for Learning and Change. These activities have been reviewed by the Mayo Clinic Conflict of Interest Review Board and are conducted in compliance with Mayo Clinic Conflict of Interest policies.

## Footnotes

## Financial and competing interests disclosure

This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and was conducted in compliance with Mayo Clinic Conflict of Interest policies. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

## Article information

Expert Rev Vaccines. Author manuscript; available in PMC 2016 Jul 1. Published in final edited form as:

Expert Rev Vaccines. 2015 Jul; 14(7): 935-947.

Published online 2015 May 2. doi: 10.1586/14760584.2015.1038249

PMCID: PMC4630804

NIHMSID: NIHMS732579

PMID: 25937189

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### Reference annotations

\* Of interest

\*\* Of considerable interest

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## Century Solutions + The Dark Side of Wheat

## Measles Scare Tactics Hurt Us All

12.9k

Posted on: Monday, February 4th 2019 at 2:15 pm Written By: Anne Mason (/gmi-blogs/annemason) Views 29238

12.2k



Originally published on www.medium.com (https://medium.com/@annemason\_86819/measles-scare-tactics-hurtus-all-5565cfe54ad5)

By the time the measles vaccine (/antitherapeutic-action/vaccination-measles) was patented in 1963 in the US, the mortality rate from measles was about 1 in 500,000.<sup>1</sup> This is less than your risk of death from falling off furniture.<sup>2</sup> Let's also consider that over 600,000 people annually die of heart disease in the US, over 500,000 people die from cancer in the US each year and over 250,000 annually die from medical errors alone.<sup>3</sup>

So why is the media reporting tiny **measles** (/disease/measles) outbreaks as if the sky itself is about to fall? Doesn't it seem as if everywhere you turn, another outbreak is reported with dire warnings that the unvaccinated are about to bring us an epidemic, the likes of which we've never seen? Kind of reminds you of the media frenzy over the Disneyland outbreak in 2014–2015, doesn't it? That's when Big Pharma focused their efforts on California and pushed through SB277, a law which removed religious and personal belief exemptions from the mandatory vaccine schedule in order for a child to attend daycare or school-public or private. Perhaps they figured that if they could manage to remove parental health choice in California, it would be a domino effect in the rest of the country.

## **Key Research Topics**

Subscribe

Disease

Asthma (/category/disease/asthma) **Chronic Illness** (/category/disease/chronic-illness) Eczema (/category/disease/eczema) Skin Diseases (/category/disease/skindiseases) Measles (/category/disease/measles) **Autism Spectrum Disorders** (/category/disease/autism-spectrumdisorders) **Vaccine-induced Toxicity** (/category/disease/vaccine-inducedtoxicity) Diabetes (/category/disease/diabetes) Heart Disease (/category/disease/heartdisease) Cancers (/category/disease/Cancers-0)

## Toxic Ingredients

Formaldehyde (/category/toxicingredients/formaldehyde) Mercury (/category/toxicingredients/mercury) Vaccine Adjuvants (/category/toxicingredients/vaccine-adjuvants) Aluminum (/category/toxicingredients/aluminum) And just in time for the start of state legislature sessions all over the country, Big Pharma has gotten the media onboard the measles terror train again. Over 70 vaccine related bills have been introduced across the country, and they are pulling out all stops to ensure that as many of their sponsored bills make it through to law.<sup>4</sup>

What's the big deal, you might ask? Well, the CDC vaccine schedule has become quite a doozy since vaccine manufacturers were released of all liability for injuries or death with the National Childhood Vaccine Injury Act in 1986.<sup>5</sup> Check out the current CDC schedule. 72 doses of vaccines by the time a child turns 18. Not quite the vaccine program of our youth. Children today are given more than 20x the doses of vaccines than my parents got. And it seems Pharma is pushing from all sides to make sure no one can avoid shooting their kids up with an insane number of doses of various cocktails of **aluminum** (/toxic-ingredient/aluminum), **formaldehyde** (/toxic-ingredient/formaldehyde), human DNA, polysorbate 80, and viruses and bacteria grown on diseased tissue.

## **VACCINES DOSES for U.S. CHILDREN**

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1000

1962	1983	2018			
TOTAL DOSES: 5	TOTAL DOSES: 24	TOTAL D	XOSES: 72		
Polio	DTP (2 months)	Influenza (pregnancy)	Influenza (18 months)		
Smallpox	OPV (2 months)	OTaP (pregnancy)	Hep A [18 months]		
DTP	OTP (4 months)	Hep 8 (birth)	influenza (30 months)		
	OPV (4 months)	Hep 8 (2 months)	Influenza (42 months)		
	DTP (6 months)	Rotavirus (2 months)	DTaP (4 years)		
	MMR (15 months)	DTaP (2 months)	IPV (4 years)		
	DTP (18 months)	HIB (2 months)	MMR (4 years)		
	OPV (18 months)	PCV (2 months)	Varicella (4 years)		
	DTP (4 years)	IPV (2 months)	Influenza (5 years)		
	OPV (4 years)	Rotavirus (4 months)	Influenza (6 years)		
	Td (15 years)	DTaP (4 months)	Influenza (7 years)		
		FIIB (4 months)	Influenza (8 years)		
		PCV (4 months)	Influenza (9 years)		
		IPV (4 months)	HPV (9 years)		
*In 1986, pharmaceutical companies producing vaccines were given full federal protection from lawsuits		Hep B (6 months)	Influenza (10 years)		
		Rotavirus (6 months)	HPV (10 years)		
		D1aP (6 months)	Influenza (11 years)		
	cine injury or death	HIB (6 months)	HPV (11 years)		
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	is if vaccines are so reed a faw to protect	IPV (6 months)	Influenza (12 years)		
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	abint p.	Influenza (7 months)	Influenza (13 years)		
	nes became HIGHLY	HIB (12 months)	Influenza (14 years)		
profitable. There are		PCV (12 months)	Influenza (15 years)		
in development, and		MMR (12 months)	Influenza (16 years)		
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pushed in r	nost stattes.	Hep A (12 months)	Influenza (17 years)		
		DTaP (18 months)	Influenza (16 years)		

Vaccines contain toxic chemicals that do NOT belong in our bodies, such as aluminum (unown to cause: brain and developmental damage even in smail doses), polysorbate 80, MSG and formaldehyde (known to cause cancer in humans).

Knowledge - Action - Health

RISK

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Misinformation abounds all over mainstream media where Big Pharma owns 70% of the advertising and therefore the narrative.<sup>6</sup> Take a look at this opinion piece in *Newsweek*, which by the way, uses a doctored stock image of a healthy baby to look as if it has what the photoshop artist thinks is measles.<sup>7</sup> It looks more like hives, but whatever. These days, accuracy is not the paramount concern for any major news outlet doing Pharma's bidding.

#### Anti-vaxiers are literally making us sick i Opinion

The State of Washington has declared an emergency because of a measles europeak in Clark County, which is across the



With the

(https://www.newsweek.com/washington-measles-outbreak-shows-anti-vaxxersare-literally-making-us-sick-1308837?

fb\_action\_ids=10157058060634224&fb\_action\_types=og.comments&fbclid=IwAR04n6OVJLShefvhCojOlLLVFynbIgre7lGfpFiD0YtBndh\_Ugi0nQ4JP\_I)

This *Newsweek* piece is one of the most egregious and absurd pieces of Big Pharma propaganda I've seen yet. It distorts and misrepresents the history and dangers of the disease, the motivations of parents who choose to avoid or delay the vaccine, and it makes blatant false statements about the risks of the **MMR vaccine** (/anti-therapeutic-action/vaccination-mumps-measles-rubella-mmr) itself. So let's dissect it a bit to illustrate my point:

The piece states that, "According to the World Health Organization, 110,000 people die every year, mostly children under the age of five. Prior to the vaccine, the U.S. also experienced the horror of measles. The CDC reports that in the 1910s, about 6,000 Americans died annually from the infection."

This is what we call truth wrapped in a distortion. First of all, the measles worldwide mortality stats are almost all the 3rd world and developing nations.<sup>•</sup> The US *did* experience "the horror of measles" mortality rates, but the article's use of "prior to the vaccine" is intended to give the false impression that the measles mortality rates "of about 6,000 Americans" were diminished by the vaccine, when in fact, the death rate had fallen to 364 deaths associated with measles the year the vaccine was introduced--50 years after "6,000 Americans were dying annually from the infection."<sup>9</sup> To put this in perspective, twice as many people die annually from falling off furniture.<sup>10</sup>

As Dr. Suzanne Humphries and Roman Bystrianyk have detailed in their data packed book, "Dissolving Illusions: Disease, Vaccines and the Forgotten History," child labor laws, sanitation, hygiene and improved standard of living and overall nutrition diminished the mortal threat of measles in the developed world--long before the vaccine even came on the scene.<sup>11</sup>

Another excerpt from the Newsweek piece is, "Another fear, that there are 'too many' vaccines, is also false. When your child crawls around on the floor licking his hands, he is exposed to far more antigens than those found in all vaccines combined."

This is designed to misinform the public about parents' concerns about vaccines and to present vaccines as no different than natural pathogens your child may be exposed to in his or her environment. This could not be further from the truth. Vaccines are injected into the body--bypassing the normal routes of entry our immune systems are designed for-- and the vaccines contain such combinations of substances and toxins like aluminum adjuvants, formaldehyde, human DNA, **mercury** (/toxic-ingredient/mercury), Polysorbate 80, and the live or attenuated bacteria or viruses which have been grown on animal organs.

Some vaccines contain more aluminum than can be considered safe for an adult male,<sup>12</sup> and the aluminum adjuvant artificially stimulates the developing baby's immune system to respond opposite the way nature intended. Dr. Suzanne Humphries explains this in detail on her website, but essentially, while an infant's immune cells have full functional capacity, they are clamped down by design during the first two years of life--in order that they learn self from non-self and also become able to differentiate between healthy, beneficial micro-organisms and those which should later be attacked.<sup>13</sup> Perhaps this derailing of the child's developing immune system is contributing to our society's huge increase in **auto-immune disorders** (/disease/autoimmune-diseases)---in which a person's body begins to attack itself---as the vaccine schedule has also increased. It may also be contributing to the alarming incidence of autism during the same time period.<sup>24</sup>

And these concerns are not just theoretical. Vaccine injury and death is more common than widely believed, and parents who have witnessed their child descend into **autism (/disease/autism-spectrum-disorders)**<sup>15</sup> or develop Type 1 diabetes,<sup>16</sup> leukemia,<sup>17</sup> bleeding disorders,<sup>18</sup> asthma, and eczema<sup>19</sup> following the MMR have become very cautious about the vaccine. It is estimated that only around 5% of vaccine adverse events are ever reported to the Vaccine Adverse Event Reporting System--as most people and many health care professionals are unaware of its existence-- but in 2016 alone, 59,117 vaccine adverse effects, 432 vaccine deaths, 1091 permanent disabilities, 4,132 vaccine hospitalizations and 10,234 vaccine emergency room visits were reported.<sup>20</sup>

And a recent study of vaccinated vs. unvaccinated children raised more concerns that vaccination is linked to **chronic illness** (/dlsease/chronic-dlsease):<sup>21</sup>



Neil Z. Miller has collected a remarkable number of studies in his thoroughly referenced "Miller's Review of Critical Vaccine Studies." His book is a wonderful resource for anyone interested in looking into these concerns and examines most of the studies referenced below--in addition to many others which suggest that natural measles infection actually protects against degenerative diseases, **skin diseases** (/disease/skin-diseases), immunoreactive diseases, asthma, allergies and certain tumors. It also looks at studies which show that measles infection in childhood may protect against childhood **leukemia** (/disease/leukemia), Hodgkin's disease, **non-Hodgkin lymphoma** (/disease/non-hodgkin-lymphoma), genital cancer, prostate cancer (/disease/prostate-cancer), gastrointestinal cancer (/disease/gastrointestinal-cancer), skin cancer (/disease/skin-cancer), iung cancer (/disease/lung-cancer), ear-nose-and throat cancers, ovarian cancer (/disease/ovarian-cancer), heart attacks (/disease/heart-attack) and strokes (/disease/stroke) during adulthood.<sup>22</sup>

This *Newsweek* piece accuses parents of spreading a "malicious lie" and "purposeful misinformation." Ascribing malice to concerned and well-researched parents is not only absurd, but deliberately inflammatory and is clearly intended to villainize parents who thoughtfully and understandably question or don't participate in the conventional vaccine program.

The piece also writes with confidence that, "Vaccines do not cause autism. This theory, which was spawned by a fraudulent get-rich scheme in the 1990s, has been shown repeatedly to be without any merit."

This is simply untrue. And absurd. Dr. Andrew Wakefield, along with other scientists and doctors, conducted a study which found a link between children's digestive and developmental issues soon after being administered the MMR vaccine. They concluded that a link with the MMR had not been proven, but that further study was warranted. That this could be described as a "get rich scheme" is laughable, and it has *not* "been shown repeatedly to be without any merit."<sup>23</sup>

This attempt at marginalizing and diminishing perfectly reasonable concerns expressed by doctors, scientists and parents, as well as vilifying anyone who questions the wisdom of the current vaccine program is not only unwarranted and unjustified, it is also remarkably stupid and unscientific. The only people profiting from such an approach are those making money from a market projected to be worth \$50.42 billion by 2023.

#### Vaccines Market worth \$50.42 billion by 2023

Based on technology, the market is segmented into conjugate vaccines, isocrivate s and a bonit demines, file attempted.

macrosoft of mich



(https://www.marketsandmarkets.com/PressReleases/vaccine-technologies.asp)

The idea that we know everything there is to know about the immune system and the consequences of an ever increasing vaccine schedule is one few would actually agree with. Let's bear this in mind as we move forward on this issue, and let's learn how to spot the propaganda when we see it. Only then will true scientific method prevail.

For additional information for natural, evidence-based interventions for measles (/disease/measles), visit the GreenMedInfo database on the subject.

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## Measles outbreak: Anti-vaccination misinformation fueled by Russian propagandists, study find

Updated Feb 12, 2019 Posted Feb 12, 2019



Anti-vaccination protesters in Olympia, Wash. (AP)



#### By Douglas Perry | The Oregonian/OregonLive

They gathered in the cold, carrying signs and grudges. One sign read: "Vaccines: the more you KNOW, the more you NO!"

With a measles outbreak among unvaccinated children in the Vancouver area causing Washington Gov. Jay Inslee to declare a health emergency last month, <u>hundreds of protesters turned out</u> at the state capitol in Olympia to oppose a bill that would restrict personal exemptions to vaccines for school-age children.



So-called "anti-vaxxers" are part of a homegrown fringe movement, one that is suspicious of scientific data about the safety and efficacy vaccinations. But they unwittingly have been getting overseas help in recent years.

Russian President Vladimir Putin isn't trying to mess only with America's elections. He has set loose his undercover opinion manipulato promote fear of vaccines and set pro- and anti-vaccination Americans against one another, a recent study concluded.

The overarching objective in this ongoing offensive: to divide and terrify Americans -- and win a second Cold War.

For the most part, Russia has taken this fight to where we live: on social media.

"Compared with average users, Russian trolls, sophisticated bots and 'content polluters' tweeted about vaccination at higher rates," the concluded last fall. The research, <u>published in the American Journal of Public Health</u>, found that "[a]ccounts masquerading as legitimat users create false equivalency, eroding public consensus on vaccination."

An example of a "disinformation" tweet: "Did you know there was a secret government database of #Vaccine-damaged child? #Vaccinal



Another tweet argued the other side: "#VaccinateUS You can't fix stupidity. Let them die from measles, and I'm for #vaccination!"

Both tweets, it appears, came from "bad actors" in Russia.

"By playing both sides, they erode public trust in vaccination, exposing us all to the risk of infectious diseases," John Hopkins University computer-science professor Mark Dredze told the BBC.

The American Journal of Public Health study linked malicious propaganda on the issue to social-media accounts from Russia's Internet Research Agency, which Robert Mueller's special-counsel office has indicted for its role in 2016 election interference.

The U.S., it must be noted, isn't the only Western country where measles outbreaks have returned in recent years. The BBC reports that rates of measles are being found throughout Europe as well.

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-- Douglas Perry

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# Lawrence Solomon: The untold story of measles

Several decades following the vaccine's introduction, the measles death rate rose, largely because the vaccine made adults, expectant mothers and infants more vulnerable

## U.S. MEASLES MORTALITY RATES

## RATE PER 100,000 POPULATION



Several decades following the vaccine's introduction, the measles death rate rose, largely because the vaccine made adults, expectant mothers and infants more vulnerable

#### LAWRENCE SOLOMON



Filed under FP Comment



Early in the last century, measles killed millions of people a year. Then, bit by bit in countries of the developed world, the death rate dropped, by the 1960s by 98% or more. In the U.K., it dropped by an astounding 99.96%. And then, the measles vaccine entered the market.

After the vaccine's introduction, the measles death rate continued to drop into the 1970s. Many scientists credit the continued decline entirely to the vaccine. Other scientists





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believe the vaccine played a minor role, if that, noting that most infectious diseases similarly petered out during the 20th century, including some, like scarlet fever, for which vaccines were never developed.

The credit for the century-long decline, scientists generally agree, goes to improved nutrition and improved health care, side effects of the West's growing affluence. In the U.S., the death rate dropped by about 98%, from about 10 per 100,000 population a century ago to one fifth of one person by 1963, the year measles vaccines made their American debut. Both before and after vaccination started, victims tended to be poor.

A study in the *American Journal of Public Health*, "Measles mortality in the United States 1971-1975," found the measles death rate to be almost 10 times higher among families whose median income was less than \$5,000 than among families whose income exceeded a modest \$10,000. Families outside metropolitan areas, who tended to have poor healthcare, had three times the death rate.

An earlier, landmark study in the *American Journal of Epidemiology* by the Center for Disease Control's Roger Barkin found similar disturbing results of measles' toll on the disadvantaged. Here race entered the picture because black children were disproportionately victimized, not by the measles virus per se but by poverty. A poor black child and a poor white child had the same high chance of dying from measles, but because white children rarely lived in abject poverty, measles claimed the blacks.

Measles didn't only discriminate by income — in another study, Barkin found that children with underlying diseases were particularly vulnerable, and that the "majority of this group were physically or mentally retarded, or both." The realization that measles was selective in whom it killed led Barkin to emphasize that vulnerable populations, rather than the general population, should be targeted for measles vaccination.

In the pre-vaccine era, when the natural measles virus infected the entire population, measles — "typically a benign childhood illness," as *Clinical Pediatrics* described it — was welcomed for providing lifetime immunity, thus avoiding dangerous adult infections. In today's vaccine era, adults have accounted for one quarter to one half of measles cases; most of them involve pneumonia, one-quarter of them hospitalization.

Also importantly, measles during pregnancies have risen dangerously because expectant mothers no longer have lifetime immunity. Today's vaccinated expectant mothers are at risk because the measles vaccine wanes with time and because it often fails to protect against measles.

A study in Houston of 12 pregnant women and one who had just given birth, all of whom had measles, found one died, seven suffered pneumonia and seven hepatitis, four went through premature labour and one lost her child in a

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Torstar swings to \$3.1-million loss as revenue falls spontaneous abortion. A study of eight measles pregnancies in Japan found three ended in spontaneous abortions or stillbirths while four babies were born with congenital measles; two mothers endured pneumonia and one hemorrhagic shock. A Los Angeles study of 58 such pregnancies found 21 ended prematurely (three induced abortions, five spontaneous abortions and 13 preterm deliveries); 35 of the 58 mothers were hospitalized, 15 contracted pneumonia, and two died.

The danger extends to babies, whose bodies are too immature to receive measles vaccination before age one, making them entirely dependent on antibodies inherited from their mothers. In their first year out of the womb, infants suffer the highest rate of measles infections and the most lasting harm. Yet vaccinated mothers have little antibody to pass on — only about one-quarter as much as mothers protected by natural measles — leaving infants vulnerable three months after birth, according to a study last year in the *Journal of Infectious Diseases*. HIV-infected children, who may account for most recent measles-related child deaths, also suffer when their mothers have been vaccinated, since HIV further reduces the antibodies they inherit.

Factors such as these increased the death rate for adults and the very young, helping to reverse the decline in deaths seen in previous decades, according to a 2004 study in the *Journal of Infectious Disease*, authored by researchers at the Centers for Disease Control and Johns Hopkins Bloomberg School of Public Health.

Vaccines for measles have had spotty safety records. Soon after their introduction, the Vital Statistics of the United States began recording deaths from the measles vaccine, along with deaths from other vaccines. By 1970, one of the two original measles vaccines was withdrawn in Canada and the U.S. after causing atypical measles syndrome, a harsh disease triggering high rates of pneumonia. In 1975, the second original vaccine was withdrawn due to 103-degrees-plus fevers, among other severe side effects. Two variants of this vaccine also proved unsatisfactory. A measles vaccine then became part of the combination MMR (measles, mumps, rubella) vaccine in the 1980s, only to be withdrawn in 1990 by Canada and in 1992 by the manufacturer after reports from Canada, the U.S., Sweden and Japan blamed MMR for febrile convulsions, meningitis, deafness and deaths. A second version of MMR, now in widespread use, is believed safe by government officials.

## TRENDING IN CANADA



Safety aside, vaccines repeatedly lailed worldwide in the 1980s and 1990s. As described in "Measles Elimination in Canada", a 2004 report authored by Canadian government officials and academics, "despite virtually 100% documented one-dose coverage in some regions, large outbreaks of measles involving thousands of cases persisted … Clearly, because of primary vaccine failure, Canada's one-dose program was insufficient."

The solution finally arrived at — adding a second dose for children — initially seemed to tame measles outbreaks. But in recent years, the new vaccination regime, too, has been failing, with widespread outbreaks again occurring, including among those who have received the recommended dose and especially among infants too young to be vaccinated, and thus unprotected because their mothers had been vaccinated. Now health experts, scrambling to find solutions, are suggesting numerous reforms, including earlier child vaccinations and second doses for adults.



Clearly, the science is not settled, making for parents a numbers game of the decision to vaccinate their children. Some parents rely on the press or health authorities to interpret the numbers. Others defy the authorities and weigh the risks in the numbers differently, in deciding what's best for their own families. Who are these others? According to a survey in *Pediatrics*, unvaccinated children in the U.S. have a mother who is at least 30 years old, who has at least one college degree and whose household has an annual income of at least \$75,000. In the absence of studies showing vaccinated children to be healthier than those unvaccinated, the parents in these educated households have determined that the numbers argue against vaccination.

Lawrence Solomon is research director of <u>Consumer Policy Institute</u>. LawrenceSolomon@nextcity.com

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## Gut Doctor "I Beg Americans To Throw Out This Vegetable Now"

## Lawrence Solomon: Vaccines can't prevent measles outbreaks

Lawrence Solomon: Measles in highly immunized societies occurs primarily among those previously immunized



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Measles in highly immunized societies occurs primarily among those previously immunized



https://business-financialpost.com/opinion/lawrence-solomon-vaccines-cant-prevent-measles-outbreaks

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### LAWRENCE SOLOMON

May 1, 2014 4:41 PM EDT

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The recent outbreaks of measles in Canada and the United States came as a shock to many public health experts but they wouldn't have to Dr. Gregory Poland, one of the world's most admired, most advanced thinkers in the field of vaccinology.

The measles vaccine has failed, he explained two years ago in a presclent paper, "The re-emergence of measles in developed countries." In that paper, he warned that due to factors that most haven't noticed, measles has come back to be a serious public health threat. Thankfully, in that paper and elsewhere he also spelled out in no-nonsense fashion what now needs to be done.

Dr. Poland is no vaccine denier. Not only is he among the harshest and most outspoken critics of the "irrationality of the antivaccinationists," he is also one of the strongest proponents for vaccines and the good that they can do. As Professor of Medicine and founder and leader of Mayo Clinic's Vaccine Research Group, one of the world's largest vaccine research organizations; as editor-in-chief of the peer-reviewed scientific journal, Vaccine; as recipient of numerous awards; as chair of vaccine data monitoring committees for pharmaceutical giant Merck; as patent holder in various vaccines processes; as someone who enjoys special employee status with the Centers for Disease Control and the U.S. Department of Defense and as someone who has sat on every federal committee that has dealt with vaccines, no one can accuse him of seeing vaccines from a narrow perspective.

And he sees the need for a major rethink, after concluding that the current measles vaccine is unlikely to ever live up to the job expected of it: "outbreaks are occurring even in highly developed countries where vaccine access, public health infrastructure, and health literacy are not significant issues. This is unexpected and a worrisome harbinger — measles outbreaks are occurring where they are least expected," he wrote in his 2012 paper, listing the "surprising numbers of cases occurring in persons who previously received one or even two documented doses of measles-containing vaccine." During the 1989-1991 U.S. outbreaks, 20% to 40% of those affected had received one to two doses. In a 2011 outbreak in Canada, "over 50% of the 98 individuals had received two doses of measles vaccine."

STORY CONTINUES BELOW











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https://business.financialpost.com/opinion/lawrence-solomon-vaccines-cant-prevent-measles-outbreaks

2/28/19, 11:46 AM Page 2 of 5 Dr. Poland noted 15 U.S. outbreaks between 2005 and 2011 and 33 in Europe in 2011 alone, involving more than 30,000 known cases. Meanwhile, the "UK has declared measles once again endemic.... such outbreaks result from both failure to vaccinate, and vaccine failure."

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People's failure to get vaccinated is deplorable, Dr. Poland often stresses. But the more fundamental problem stems from the vaccine being less effective in real life than predicted, with a too-high failure rate — between 2% and 10% don't develop expected antibodies after receiving the recommended two shots. Because different people have different genetic makeups, the vaccine is simply a dud in many, failing to provide the protection they think they've

## FINANCIAL POST

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Devon Energy, with up to \$9 billion in assets here, is getting out of Canada's oilsands general population thought necessary to protect public health. For example, 9% of children having two doses of the vaccine, as public health authorities now recommend, will have lost their immunity after just seven and a half years. As more time passes, more lose their immunity. "This leads to a paradoxical situation whereby measles in highly immunized societies occurs primarily among those previously immunized," Dr. Poland stated.

The measles vaccine's inadequacy doesn't end there, however. It "cannot be administered to those who are immunocompromised, who have allergies to vaccine components, or who are pregnant [among other limitations, leaving] a large enough segment of the population susceptible and unprotected from measles such that cases will continue to occur."

The answer, according to Dr. Poland, lies in our genes. Because of their genetic predisposition, some people will not respond to the current measles vaccine, even with additional boosters. By the same token, the genetic predisposition of others makes them susceptible to harm from the measles vaccine, leading to public wariness, including among the well educated. What is needed, suggests Dr. Poland, is for the public health establishment to accept that the current measles vaccine has so many drawbacks as to make it





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'Long overdue': Devon Energy late to the party in selling off oilsands assets



Investors sensing a Warren Buffett moment in SNC Lavalin should look before they leap unworkable, and get on with the job of developing next-generation vaccines.

This next generation vaccine technology, which his Mayo Clinic group is helping pioneer, marries vaccinology with genomics to create personalized, rather than one-size-fits-all, vaccines. Through this new medical discipline of "vaccinomics," a term he dubbed, medical science will not only have the wherewithal to finally achieve the decades-long dream of eradicating measles and other diseases, he believes, but will also do so at lower cost while addressing the concerns of the educated public.

As I will discuss in part two of this series next week, vaccinomics is no pie-inthe-sky fantasy but possibly the next big coming thing, well worth pursuing, and well worth the investment in its development that will be required.

Lawrence Solomon is research director of <u>Consumer Policy Institute</u>. LawrenceSolomon@nextcity.com

For Lawrence's Solomon's recent column, The untold story of measles, click here.

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incentive payment will first rebalance owing for the year, increase any refund

## COMMENTS







# OREGON LAW REVIEW

2014

VOLUME 93 NUMBER 1

Articles

## MARY HOLLAND AND CHASE E. ZACHARY\*

## Herd Immunity and Compulsory Childhood Vaccination: Does the Theory Justify the Law?

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<sup>\*</sup> Mary Holland is a Research Scholar and Director of the Graduate Lawyering Program at New York University School of Law. Chase Zachary received his J.D. degree from NYU School of Law in 2014, and he has a Ph.D. in Chemistry from Princeton University. The authors may be reached at the NYU School of Law, 40 Washington Square South, 107 Vanderbilt Hall, New York, NY 10012, mary.holland@nyu.edu and czachary@nyu.edu. They would like to thank Mark Blaxill, James Holland, Patricia Rawlinson, Jenny Roberts, Juliet Stumpf, Eva Vanamee, and several anonymous reviewers for their helpful comments. They also thank Jesus Ballivian for valuable administrative support.

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Herd Immunity and Compulsory Childhood Vaccination: Does the Theory Justify the Law?

## ABSTRACT

Compulsory childhood vaccination is a cornerstone of U.S. public health policy. All fifty states compel children to vaccinate against many infectious diseases to achieve so-called herd immunity, a scientific theory that attempts to explain how societies protect themselves against infectious disease.

This Article explores both the theory and practice of herd immunity. The authors evaluate the scientific assumptions underlying the theory, how the theory applies in law, a game theory approach to herd immunity, and a possible framework for rational policymaking. The Article argues that *herd immunity* is unattainable for most diseases and is therefore an irrational goal. Instead, the authors conclude that *herd effect* is attainable and that a voluntary vaccination marketplace, not command-and-control compulsion, would most efficiently achieve that goal.

The Article takes on the bugaboo of the citizen "free rider" who is out to game the system, how a vaccination marketplace might work, and what factors policymakers must take into account in developing sound policies. The Article concludes that it is time for states to adopt more realistic and cost-efficient laws to achieve attainable herd effect, not illusory herd immunity.

## INTRODUCTION

Mon the theory of herd immunity.<sup>1</sup> The theory describes a form of indirect protection in which non-immune individuals are protected from those that have acquired a disease and recovered.<sup>2</sup> Promoters of

3

<sup>&</sup>lt;sup>1</sup> See James G. Hodge, Jr. & Lawrence O. Gostin, School Vaccination Requirements: Historical, Social, and Legal Perspectives, 90 Ky. L.J. 831, 833 (2002) ("Each state has school vaccination laws which require children of appropriate age to be vaccinated for several communicable diseases." (citation omitted)); see also State Information, IMMUNIZATION ACTION COALITION, http://www.immunize.org/laws (last visited Mar. 6, 2014) (showing vaccination mandates by state, and while the Immunization Action Coalition is solely responsible for this website, its information is based on government sources, and the website is funded in part by the Centers for Disease Control and Prevention).

<sup>&</sup>lt;sup>2</sup> See, e.g., Paul Fine et al., "Herd Immunity": A Rough Guide, 52 CLINICAL INFECTIOUS DISEASES 911 (2011) [hereinafter Fine, Rough Guide]; Paul E.M. Fine, Herd Immunity: History, Theory, Practice, 15 EPIDEMIOLOGIC REVS. 265 (1993) [hereinafter Fine, History]; John P. Fox et al., Herd Immunity: Basic Concept and Relevance to Public Health Immunization Practices, 94 J. EPIDEMIOLOGY 179 (1971).

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significant relationship, at the ninety-five percent confidence level, between measures of non-medical childhood disease exemptions and disease incidence rates in the fifty states.<sup>274</sup> Although several open issues of their study remain for the scientific literature to consider,<sup>275</sup> their empirically-based study results strongly reinforce the view that herd immunity should not be the *de facto* objective of vaccination policy.

A voluntary approach to maximizing herd effect ensures efficiency of the vaccination marketplace and preserves individual choice. Policymakers should reconsider the appropriate level of regulation of the vaccination market, explicitly balancing the costs of vaccination coverage with the expected benefits from a particular vaccination program.<sup>276</sup>

## CONCLUSION AND RECOMMENDATIONS

Herd immunity is generally unattainable in the real world because key assumptions, like population homogeneity, do not exist and because current vaccine technology is imperfect. Vaccination programs should therefore aim to achieve herd effect, not herd immunity and concomitantly, disease control rather than eradication.

The free rider problem is a red herring. The Bauch-Earn game theory analysis and experience suggest that it does not drive individual decision making in the real world.<sup>277</sup> If safe and effective vaccines are available, most people will voluntarily accept the risks of vaccination rather than the potential risks of serious infectious disease.

Market forces will naturally lead to an equilibrium point for vaccination; mandates to increase coverage above the equilibrium point yield little or no marginal gains in the absence of obtainable herd immunity. Vaccination programs should therefore focus on "soft" regulation by investing in safer and more efficacious vaccine

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<sup>&</sup>lt;sup>274</sup> Yang & Debold, *supra* note 14, at 374–76.

<sup>&</sup>lt;sup>275</sup> Id. at 375.

<sup>&</sup>lt;sup>276</sup> See OFFICE OF MGMT. & BUDGET, supra note 8, at 9–10 (noting that an agency "should also perform a [benefit-cost analysis] for major health and safety rulemakings to the extent that valid monetary values can be assigned to the primary expected health and safety outcomes[,]" and that even "[i]f the non-quantified benefits and costs are likely to be important, [the agency] should recommend which of the non-quantified factors are of sufficient importance to justify consideration in the regulatory decision").

<sup>&</sup>lt;sup>277</sup> Bauch & Earn, *supra* note 244, at 13393-94.
#### 2014] Herd Immunity and Compulsory Childhood Vaccination: Does the Theory Justify the Law?

technology, ensuring informed consent and opening lines of communication between parents, physicians, and policymakers.

These conclusions lead to the following specific recommendations for U.S. federal and state vaccine policy makers. First, federal and state vaccination programs should acknowledge that the goal of vaccine policy is to control disease, not eradicate it. Effective programs should focus on creating herd effect, not herd immunity, and take into account all the economic costs and health risks of vaccination.

Second, states should experiment with market-based approaches to vaccination, freeing resources otherwise devoted to compliance to other healthcare needs. States can change mandates to recommended or elective programs with relative ease and observe what consequences follow. States can start by removing those vaccination mandates that have inadequate public health rationales, such as the mandate for tetanus, which is non-contagious, and for hepatitis B, which is primarily sexually transmitted and a disease for which children are at low risk.

Third, states should ensure that vaccine consumers receive complete information to make rational choices. States can impose higher informational requirements than current federal law. Under federal law, parents are required to receive only minimal information on vaccination benefits and risks.<sup>278</sup> States should require that parents or guardians receive all the information they would otherwise obtain with any prescription drug.

Parents can and should be able to determine their own children's best interests and voluntarily choose vaccines based on complete and accurate information. Prior, free, and informed consent is the hallmark of modern ethical medicine.<sup>279</sup> The "choice" between fulfilling a child's vaccination mandates or foregoing her education is

\*\*\*

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<sup>&</sup>lt;sup>278</sup> 42 U.S.C. § 300aa—26 (2012) (describing the Vaccine Information Statements that the CDC now produces); *see Vaccine Information Statements*, CTRS. FOR DISEASE CONTROL & PREVENTION, http://www.cdc.gov/vaccines/hcp/vis/index.html?s\_cid=cs\_000 (last updated June 11, 2014).

<sup>&</sup>lt;sup>279</sup> Universal Declaration on Bioethics and Human Rights, UNITED NATIONS EDUC., SCIENTIFIC, AND CULTURAL ORG. (UNESCO), at art. 6 (2005), unesdoc.unesco.org /images/0014/001461/146180e.pdf ("Any preventive, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information.").

#### OREGON LAW REVIEW

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scarcely a voluntary choice; it is a coerced choice at best. Because public health policies have not attained herd immunity for any childhood disease despite sixty years of compulsory policies and intensive effort, it seems both logical and wise to recalculate our policies. It is time to abandon the illusion of herd immunity through compulsion and to adopt realistic and respectful policies to achieve herd effect based on parents' informed choices.

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### FEBRUARY 06, 2019 CDC, Check YOUR Data: MMR Vaccination Rates are NOT Declining



#### By JB Handley, Children's Health Defense Director and Co-Founder of Generation Rescue

There's a narrative being spread that the vaccination rate for the MMR vaccine has fallen lately due to irresponsible parents, and that the only way to fix the declining rate is to tighten up vaccine exemption laws in every state, which led me to ask a fairly obvious question about my home state: "What has the MMR vaccination rate in Oregon been over time (and why can't I find that in any of the hysterical media)?" Luckily, the CDC has a super-easy, interactive map that answers this question very clearly, and I hope any members of the media with a brain start to take a look at the actual data, I took a screenshot of Oregon's and you better take a screenshot of your state's before the CDC takes down this weblink:

https://www.cdc.gov/.../chi.../datareports/mmr/trend/index.html

### So, what the heck is going on?

### #wheresthedecline?

#### ChildVaxView

Measles, mumps, and rubella (MMR) vaccination coverage among children 19-35 months by State, HHS Region, and the United States, National Immunization: Survey-Child (NIS-Child), 1995 through 2017



Why is the media saying that parents aren't vaccinating and therefore measles is making a comeback? Let me explain:

- The media abuses the vaccine exemption number, not the MMR vaccination number. Parents file exemptions anytime they don't get EVERY vaccine required for school for their child. In Oregon, if you get 0 of 24 or 23 of 24 vaccines required for school for your child, you are counted as "exempt."
- 2. What the Oregon Health Authority knows, and is true in every other state, is that exemptions go up when one

thing happens: new vaccines are added to the required school schedule. Quoting the Oregon Health Authority who wrote: "When other vaccines have been added as school immunization requirements, non-medical exemption rates have increased for all vaccines." Why would that happen? Two reasons: 1. Administrative burden, and 2. Wariness of brand new vaccine requirements (like, "does my kid really need Hep A?".)



So, basically, here's how it works: abuse and misinterpret a rising exemption number–guaranteed to go up if you add new vaccine requirements to the schedule–and generalize that it's happening for all vaccines. Then, NEVER show the historical data, because it decimates your story.

I hope state activists grab the data for their state, share it with their legislators, and ask a simple question:

### "Where's the decline?"

Since Washington State is facing an exemption fight, l grabbed a screen shot of WA data. Why can't people just be honest about the data? #wheresthedecline

#### ChildVaxV ew

Yulea User Caldes Hieleand User Goule 🚆 💷 an - I Mettlade and Innitations (Downland Report Data (2017 Report ) 2017 Dishborra

Measles, mumps, and rubella (MMR) vaccination coverage among children 19-35 months by State, HHS Region, and the United States, National Immunization Survey-Child (NIS-Child), 1995 through 2017



I also pasted below a table of Oregon's actual numbers, from 1995 to 2017, please show me where the material decline happened (from year to year, there will be some natural variation, because this is a survey.)

Measles, mumps, and rubella (MMR) vaccination coverage among children 19-35 months STATE OF OREGON, National Immunization Survey-Child (NIS-Child), 1995 through 2017

YEAR	MMR coverage level			
1995	87.6			
1996	85.3			
1997	87.4			
1998	88.6			
1999	85.6			
2000	90.3			
2001	88.4			
2002	86.6			
2003	92.4			
2004	93.7			
2005	82.7			
2006	88.7			
2007	88.9			
2008	92.0			
2009	88.1			
2010	92.8			
2011	90.6			
2012	87.3			
2013	89.4			
2014	85.1			
2015	94.1			
2016	86.7			
2017	90.3			

Source: https://www.cdc.gov/vaccines/imz-managers/coverage/childvaxview/data-reports/mmr/trend/index.html

### Truthful Data Destroys the False Narrative

Note: this data above is for children, aged 19-35 months. By the time these kids get into school, the vaccination rate goes even higher. What's so important about all this data is that it destroys the false narrative. Vaccination rates haven't gone down lately. Period. Ask any epidemiologist you know to run these numbers. The trend lines are ALL flat. Since 1995. I also know that each year, here in Oregon, the OHA's data and the NIS data from CDC are generally the same, so I'd love to see OHA produce the MMR vaccination rate data since 1995 and ask them a simple question: why not tell the truth?

When I looked at the CDC's numbers, it clearly showed that the MMR vaccination rate has held steady for more than 20 years. I wanted to make sure and corroborate that data with data from the Oregon Health Authority, which they conveniently don't publish very often, but someone sent me their data from 2014, showing that 97.1% of 7<sup>th</sup> graders in Oregon have received an MMR vaccine! **Where's the decline?** 



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### 1995 through 2017 Childhood Measles, Mumps, and Rubella (MMR) Vaccination Coverage **Trend Report**

Back to ChildVaxView Interactive! main page



Video User Guides (https://www2.cdc.gov/vaccines/ed/vaxview tutorials/c v t/c v t.html) | Help and User Guide [4 pages] Methods and Limitations | Download Report Data (https://ndmsia.cdc.gov/IAS/data/excel?viewId=2116&geoId=17&subsetId=&viewer=Excel) | 2017 Report | 2017 Dashboard

Measles, mumps, and rubella (MMR) vaccination coverage among children 19-35 months by State, HHS Region, and the United States, National Immunization Survey-Child (NIS-Child), 1995 through 2017



#### ∧ <u>Top of Page</u>

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- For Specific Groups (/vaccines/imz-managers/coverage/childvaxview/groups/index.html)
  - ÷

#### File Formats Help:

How do I view different file formats (PDF, DOC, PPT, MPEG) on this site? (https://www.cdc.gov/Other/plugins/)

(https://www.cdc.gov/Other/plugins/#pdf)

Page last reviewed: October 11, 2018 Page last updated: October 11, 2018







Dr. Tetyana Obukhanych

### An Open Letter to Legislators Currently Considering Vaccine Legislation from Tetyana Obukhanych, PhD

Dear Legislator:

My name is Tetyana Obukhanych. I hold a PhD in Immunology. I am writing this letter in the hope that it will correct several common misperceptions about vaccines in order to help you formulate a fair and balanced understanding that is supported by accepted vaccine theory and new scientific findings.

### Do unvaccinated children pose a higher threat to the public than the vaccinated?

It is often stated that those who choose not to vaccinate their children for reasons of conscience endanger the rest of the public, and this is the rationale behind most of the legislation to end vaccine exemptions currently being considered by federal and state legislators country-wide.

You should be aware that the nature of protection afforded by many modern vaccines – and that includes most of the vaccines

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100 Percent of Oat Products Tested Positive for Weedkiller Glyphosate recommended by the CDC for children – is not consistent with such a statement.

I have outlined below the recommended vaccines that cannot prevent transmission of disease either because they are not designed to prevent the transmission of infection (rather, they are intended to prevent disease symptoms), or because they are for non-communicable diseases.

People who have not received the vaccines mentioned below pose no higher threat to the general public than those who have, implying that discrimination against non-immunized children in a public school setting may not be warranted.

1. IPV (inactivated poliovirus vaccine) cannot prevent transmission of poliovirus. (see appendix for the scientific study, Item #1). Wild poliovirus has been non-existent in the USA for at least two decades. Even if wild poliovirus were to be reimported by travel, vaccinating for polio with IPV cannot affect the safety of public spaces. Please note that wild poliovirus eradication is attributed to the use of a different vaccine, OPV or oral poliovirus vaccine. Despite being capable of preventing wild poliovirus transmission, use of OPV was phased out long ago in the USA and replaced with IPV due to safety concerns.

2. Tetanus **is not a contagious disease**, but rather acquired from deep-puncture wounds contaminated with C. tetani spores. Vaccinating for tetanus (via the DTaP combination vaccine) cannot alter the safety of public spaces; it is intended to render personal protection only.

3. While intended to prevent the disease-causing effects of the diphtheria toxin, **the diphtheria toxoid vaccine** (also contained in the DTaP vaccine) **is not designed to prevent colonization and transmission of** *C. diphtheriae*. Vaccinating for diphtheria cannot alter the safety of public spaces; it is likewise intended for personal protection only.

4. The acellular pertussis (aP) vaccine (the final element of the DTaP combined vaccine), now in use in the USA, replaced the whole cell pertussis vaccine in the late 1990s, which was followed by an unprecedented resurgence of whooping cough. An

16,046 Views



Arizona Cardiologist Responds to Critics Regarding Measles and Vaccines

10,522 Views



U.S. Government: DNA Collected from Newborn Dried Blood Spots No Longer Protected From Being Used in Human Research

10,150 Views



The Next Mandatory Vaccine Battleground:

experiment with deliberate pertussis infection in primates revealed that the aP vaccine is not capable of preventing colonization and transmission of B. pertussis. The FDA has issued a warning regarding this crucial finding. [1]

Furthermore, the 2013 meeting of the Board of Scientific Counselors at the CDC revealed additional alarming data that **pertussis variants (PRN-negative strains) currently circulating in the USA acquired a selective advantage to infect those who are up-to-date for their DTaP boosters**, meaning that people who are up-to-date are *more* likely to be infected, and thus contagious, than people who are not vaccinated.

5. Among numerous types of *H. influenzae*, the Hib vaccine covers only type b. Despite its sole intention to reduce symptomatic and asymptomatic (disease-less) Hib carriage, **the introduction of the Hib vaccine has inadvertently shifted strain dominance towards other types of H. influenzae (types a through f)**. These types have been causing invasive disease of high severity and increasing incidence in adults in the era of Hib vaccination of children (see appendix for the scientific study, Item #4). The general population is more vulnerable to the invasive disease now than it was prior to the start of the Hib vaccination campaign. Discriminating against children who are not vaccinated for Hib does not make any scientific sense in the era of non-type b *H. influenzae* disease.

6. **Hepatitis B is a blood-borne virus.** It does not spread in a community setting, especially among children who are unlikely to engage in high-risk behaviors, such as needle sharing or sex. Vaccinating children for hepatitis B cannot significantly alter the safety of public spaces. Further, school admission is not prohibited for children who are chronic hepatitis B carriers. To prohibit school admission for those who are simply unvaccinated – and do not even carry hepatitis B – would constitute unreasonable and illogical discrimination.

In summary, a person who is not vaccinated with IPV, DTaP, HepB, and Hib vaccines due to reasons of conscience poses no extra danger to the public than a person who is. No discrimination is warranted. Homeschool Children

5,988 Views



Why I don't Vaccinate My Dogs At All

3,864 Views

# Who Owns Organics?

America's Fraudulent Organics Industry: 40% of All Organic Food Tested Positive for Prohibited Pesticides

3,216 Views



20,000 Satellites for 5G to be Launched Sending Focused Beams o

#### How often do serious vaccine adverse events happen?

It is often stated that vaccination rarely leads to serious adverse events.

Unfortunately, this statement is not supported by science.

A recent study done in Ontario, Canada, established that vaccination actually leads to an emergency room visit for 1 in 168 children following their 12-month vaccination appointment and for 1 in 730 children following their 18month vaccination appointment (see appendix for a scientific study, Item #5).

When the risk of an adverse event requiring an ER visit after wellbaby vaccinations is demonstrably so high, vaccination must remain a choice for parents, who may understandably be unwilling to assume this immediate risk in order to protect their children from diseases that are generally considered mild or that their children may never be exposed to.

Can discrimination against families who oppose vaccines for reasons of conscience prevent future disease outbreaks of communicable viral diseases, such as measles?

Measles research scientists have for a long time been aware of the "measles paradox." I quote from the article by Poland & Jacobson (1994) "Failure to Reach the Goal of Measles Elimination: Apparent Paradox of Measles Infections in Immunized Persons." Arch Intern Med 154:1815-1820:

"The apparent paradox is that as measles immunization rates rise to high levels in a population, measles becomes a disease of immunized persons." [2]

Further research determined that behind the "measles paradox" is a fraction of the population called LOW VACCINE RESPONDERS. Low-responders are those who respond poorly to the first dose of the measles vaccine. These individuals then mount a weak immune response to subsequent RE-vaccination and quickly return to the pool of "susceptibles" within 2-5 years, despite being fully vaccinated. [3] Intense Microwave Radiation Over Entire Earth

2,731 Views



States Move to Mandate Deadly HPV Gardasil Vaccine for Children

2,036 Views

Re-vaccination cannot correct low-responsiveness: it appears to be an immuno-genetic trait. [4] The proportion of low-responders among children was estimated to be 4.7% in the USA. [5]

Studies of measles outbreaks in Quebec, Canada, and China attest that **outbreaks of measles still happen, even when vaccination compliance is in the highest bracket** (95-97% or even 99%, see appendix for scientific studies, Items #6&7). This is because even in high vaccine responders, vaccine-induced antibodies wane over time. Vaccine immunity does not equal lifelong immunity acquired after natural exposure.

It has been documented that vaccinated persons who develop breakthrough measles are contagious. In fact, two major measles outbreaks in 2011 (in Quebec, Canada, and in New York, NY) were re-imported by previously vaccinated individuals. [6] [7]

Taken together, these data make it apparent that elimination of vaccine exemptions, currently only utilized by a small percentage of families anyway, will neither solve the problem of disease resurgence nor prevent re-importation and outbreaks of previously eliminated diseases.

### Is discrimination against conscientious vaccine objectors the only practical solution?

The majority of measles cases in recent US outbreaks (including the recent Disneyland outbreak) are adults and very young babies, whereas in the pre-vaccination era, measles occurred mainly between the ages 1 and 15.

Natural exposure to measles was followed by lifelong immunity from re-infection, whereas vaccine immunity wanes over time, leaving adults unprotected by their childhood shots. Measles is more dangerous for infants and for adults than for school-aged children.

Despite high chances of exposure in the pre-vaccination era, measles practically never happened in babies much younger than one year of age due to the robust maternal immunity transfer mechanism. The vulnerability of very young babies to measles today is the direct outcome of the prolonged mass vaccination campaign of the past, during which their mothers, themselves vaccinated in their childhood, were not able to experience measles naturally at a safe school age and establish the lifelong immunity that would also be transferred to their babies and protect them from measles for the first year of life.

Luckily, a therapeutic backup exists to mimic now-eroded maternal immunity. Infants as well as other vulnerable or immunocompromised individuals, are eligible to receive immunoglobulin, a potentially life-saving measure that supplies antibodies directed against the virus to prevent or ameliorate disease upon exposure (see appendix, Item #8).

#### In summary:

1) due to the properties of modern vaccines, non-vaccinated individuals pose no greater risk of transmission of polio, diphtheria, pertussis, and numerous non-type b H. influenzae strains than vaccinated individuals do, non-vaccinated individuals pose virtually no danger of transmission of hepatitis B in a school setting, and tetanus is not transmissible at all;

2) there is a significantly elevated risk of emergency room visits after childhood vaccination appointments attesting that vaccination is not risk-free;

3) outbreaks of measles cannot be entirely prevented even if we had nearly perfect vaccination compliance; and

4) an effective method of preventing measles and other viral diseases in vaccine-ineligible infants and the immunocompromised, immunoglobulin, is available for those who may be exposed to these diseases.

Taken together, these four facts make it clear that discrimination in a public school setting against children who are not vaccinated for reasons of conscience is completely unwarranted as the vaccine status of conscientious objectors poses no undue risk to the public.

Sincerely Yours,

~ Tetyana Obukhanych, PhD

**Tetyana Obukhanych** earned her Ph.D. in Immunology at the Rockefeller University, New York, NY with her research dissertation focused on immunologic memory. She was subsequently involved in laboratory research as a postdoctoral research fellow at Harvard Medical School and Stanford University School of Medicine, before fully devoting herself to natural parenting.

(Original Source: legislature.vermont.gov – Testimony Senate Health & Welfare Committee Wednesday April 22, 2015 H.98 – public records)

**Editor's Note**: This article has been slighted edited to reflect the language from the letter submitted to the *Vermont General Assembly* on April 22, 2015. As part of the *Vermont Senate Health & Welfare Committee*, it is a matter of public record and accessible here.)

**UPDATE**: The above links on the Vermont government website no longer work. Here is a copy.



Comment on this article at VaccineImpact.com.

#### Appendix

Item #1. The Cuba IPV Study collaborative group. (2007) Randomized controlled trial of inactivated poliovirus vaccine in Cuba. N Engl J Med 356:1536-44

### http://www.ncbi.nlm.nih.gov/pubmed/17429085

The table below from the Cuban IPV study documents that 91% of children receiving no IPV (control group B) were colonized with live attenuated poliovirus upon deliberate experimental inoculation. Children who were vaccinated with IPV (groups A and C) were similarly colonized at the rate of 94-97%. High counts of live virus were recovered from the stool of children in all groups. These results make it clear that IPV cannot be relied upon for the control of polioviruses.

Group	No. of Infants	Туре І		Type 2		Туре 3		Any Type of Poliovirus		
		No	(95)にて()	No.	$\approx (25\% C)$	No.	% (95% Ci)	No.	% (R5% CI)	Mean Log <sub>10</sub> Titer in Fecal Sample (95% Ci)
Δ	52	10	19 (10~33)	41	87 (74-94)	5.	10(3-21)	4.6	(4 (84-99)	3.46 (3.12-3.25)
15	5.4	9	17 (6-29)	48	89 (77-96)	1	6 (2-15)	(49)	91 (80-97)	3.89 (3 54-4 14)
Ç.	72.	13	18 (10-29)	6.7	93 (25-98)	10	14 (7-74)	/0	57 (90-200)	3 37 (3 14-3 60)

are based on the binomial distribution

[ Group A received a combination of diphtherial percussis-tetanus vaccine, Hiermania's influenzer type b vaccine, and inactivated policy rus-vaccine (DPT-Hib-IPV) at 6, 10, and 14 weeks of age. Group 6, the control group, received a combination of DPT fraccine and Hib vaccine at 6, 10, and 14 weeks. Group C received the DPT-Hib-IPV combination at 8 and 16 weeks. I Mean values are given for exceeders of policy russ.

Item #2. Warfel et al. (2014) Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model. Proc Natl Acad Sci USA 111:787-92

#### http://www.ncbi.nlm.nih.gov/pubmed/24277828

"Baboons vaccinated with aP were protected from severe pertussis-associated symptoms but not from colonization, did not clear the infection faster than naïve [unvaccinated] animals, and readily transmitted B. pertussis to unvaccinated contacts. By comparison, previously infected [naturally-immune] animals were not colonized upon secondary infection."

Item #3. Meeting of the Board of Scientific Counselors, Office of Infectious Diseases, Centers for Disease Control and Prevention, Tom Harkins Global Communication Center, Atlanta, Georgia, December 11-12, 2013

### http://www.cdc.gov/maso/facm/pdfs/BSCOID/2013121112\_BSCOID\_Minutes.pdf

#### Resurgence of Pertussis (p.6)

"Findings indicated that 85% of the isolates [from six Enhanced Pertussis Surveillance Sites and from epidemics in Washington and Vermont in 2012] were PRN-deficient and vaccinated patients had significantly higher odds than unvaccinated patients of being infected with PRN-deficient strains. Moreover, when patients with up-to-date DTaP vaccinations were compared to unvaccinated patients, the odds of being infected with PRNdeficient strains increased, suggesting that PRN-bacteria may have a selective advantage in infecting DTaP-vaccinated

persons."

Item #4. Rubach *et al.* (2011) **Increasing incidence of invasive** *Haemophilus influenzae* disease in adults, Utah, USA. *Emerg Infect Dis* 17:1645-50

http://www.ncbi.nlm.nih.gov/pubmed/21888789

The chart below from Rubach *et al.* shows the number of invasive cases of *H. influenzae* (all types) in Utah in the decade of childhood vaccination for Hib.



Item #5. Wilson *et al.* (2011) Adverse events following 12 and 18 month vaccinations: a population-based, self-controlled case series analysis. *PLoS One* 6:e27897

#### http://www.ncbi.nlm.nih.gov/pubmed/22174753

"Four to 12 days post 12 month vaccination, children had a 1.33 (1.29-1.38) increased relative incidence of the combined endpoint compared to the control period, or at least one event during the risk interval for every 168 children vaccinated. Ten to 12 days post 18 month vaccination, the relative incidence was 1.25 (95%, 1.17-1.33) which represented at least one excess event for every 730 children vaccinated. The primary reason for increased events was statistically significant elevations in emergency room visits following all vaccinations."

Item #6. De Serres et al. (2013) Largest measles epidemic in

https://healthimpactnews.com/2017/harvard-immunologist-to-In\_I0rlK-ImgXe08eUKHY/J0SfTacJihotrnK0-DIAUoNaobolKAwJ-IOU

North America in a decade–Quebec, Canada, 2011: contribution of susceptibility, serendipity, and superspreading events. *J Infect Dis* 207:990-98

http://www.ncbi.nlm.nih.gov/pubmed/23264672

"The largest measles epidemic in North America in the last decade occurred in 2011 in Quebec, Canada."

"A super-spreading event triggered by 1 importation resulted in sustained transmission and 678 cases."

"The index case patient was a 30-39-year old adult, after returning to Canada from the Caribbean. The index case patient received measles vaccine in childhood."

"Provincial [Quebec] vaccine coverage surveys conducted in 2006, 2008, and 2010 consistently showed that by 24 months of age, approximately 96% of children had received 1 dose and approximately 85% had received 2 doses of measles vaccine, increasing to 97% and 90%, respectively, by 28 months of age. With additional first and second doses administered between 28 and 59 months of age, population measles vaccine coverage is even higher by school entry."

"Among adolescents, 22% [of measles cases] had received 2 vaccine doses. Outbreak investigation showed this proportion to have been an underestimate; active case finding identified 130% more cases among 2-dose recipients."

Item #7. Wang *et al.* (2014) **Difficulties in eliminating measles** and controlling rubella and mumps: a cross-sectional study of a first measles and rubella vaccination and a second measles, mumps, and rubella vaccination. *PLoS One* 9:e89361

http://www.ncbi.nlm.nih.gov/pubmed/24586717

"The reported coverage of the measles-mumps-rubella (MMR) vaccine is greater than 99.0% in Zhejiang province. However, the incidence of measles, mumps, and rubella remains high."

#### Item #8. Immunoglobulin Handbook, Health Protection Agency

http://webarchive.nationalarchives.gov.uk/20140714084352/http://www.hpa.org.uk/webc/HPAw

### HUMAN NORMAL IMMUNOGLOBULIN (HNIG):

Indications

- 1. To prevent or attenuate an attack in immuno-compromised contacts
- 2. To prevent or attenuate an attack in pregnant women
- To prevent or attenuate an attack in infants under the age of 9 months

#### Footnotes

[1] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm376937.htm

### (Edited to add: Apparently, the FDA pulled the above link, but the content is archived here:

https://web.archive.org/web/20131130004447/https://www.fda.gov/NewsEvents/Newsroom/Pre

[2] http://archinte.jamanetwork.com/article.aspx?articleid=619215

### [3] Poland (1998) Am J Hum Genet 62:215-220

http://www.ncbi.nlm.nih.gov/pubmed/9463343

" 'poor responders,' who were re-immunized and developed poor or low-level antibody responses only to lose detectable antibody and develop measles on exposure 2–5 years later."

[4] *ibid* 

"Our ongoing studies suggest that seronegativity after vaccination [for measles] clusters among related family members, that genetic polymorphisms within the HLA [genes] significantly influence antibody levels."

### [5] LeBaron et al. (2007) Arch Pediatr Adolesc Med 161:294-301

"Titers fell significantly over time [after second MMR] for the study population overall and, by the final collection, 4.7% of children were potentially susceptible."

### [6] De Serres et al. (2013) J Infect Dis 207:990-998

http://www.ncbi.nlm.nih.gov/pubmed/23264672

"The index case patient received measles vaccine in childhood."

### [7] Rosen et al. (2014) Clin Infect Dis 58:1205-1210

http://www.ncbi.nlm.nih.gov/pubmed/24585562

"The index patient had 2 doses of measles-containing vaccine."

### Say NO to Mandatory Vaccines T-Shirt



Leaving a lucrative career as a nephrologist (kidney doctor), Dr. Suzanne Humphries is now free to actually help cure people. In this autobiography she explains why good doctors are constrained within the current corrupt medical system from practicing real, ethical medicine. FREE Shipping Available! Order here.

### Medical Doctors Opposed to Forced Vaccinations – Should Their Views be Silenced?

2/26/19, 11:39 AM Page 16 of 20 Medical Doctors Opposed to Forced Vaccinations Should Their Views be Silenced?



eBook – Available for immediate download.

One of the biggest myths being propagated in the compliant mainstream media today is that doctors are either pro-vaccine or anti-vaccine, and that the anti-vaccine doctors are all "guacks."

However, nothing could be further from the truth in the vaccine debate. Doctors are not unified at all on their positions regarding "the science" of vaccines, nor are they unified in the position of removing informed consent to a medical procedure like vaccines.

The two most extreme positions are those doctors who are 100% against vaccines and do not administer them at all, and those doctors that believe that ALL vaccines are safe and effective for ALL people, ALL the time, by force if necessary.

Very few doctors fall into either of these two extremist positions, and yet it is the extreme pro-vaccine position that is presented by the U.S. Government and mainstream media as being the dominant position of the medical field.

In between these two extreme views, however, is where the vast majority of doctors practicing today would probably categorize their position. Many doctors who consider themselves "provaccine," for example, do not believe that every single vaccine is appropriate for every single individual. Many doctors recommend a "delayed" vaccine schedule for some patients, and not always the recommended one-size-fits-all CDC childhood schedule. Other doctors choose to recommend vaccines based on the actual science and merit of each vaccine, recommending some, while determining that others are not worth the risk for children, such as the suspect seasonal flu shot.

These doctors who do not hold extreme positions would be opposed to government-mandated vaccinations and the removal of all parental exemptions.

In this eBook, I am going to summarize the many doctors today who do not take the most extremist pro-vaccine position, which is probably not held by very many doctors at all, in spite of what the pharmaceutical industry, the federal government, and the mainstream media would like the public to believe.

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### Medical Doctors Opposed to Forced Vaccinations – Should Their Views be Silenced?

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### FAQS: THE MEASLES, MUMPS AND RUBELLA (MMR) VACCINE VS. MEASLES

#### P\$C PHYSICIANS FOR INFORMED CONSENT

### Answers to questions about the risks of the MMR vaccine vs. the risks of measles in the United States

With data, statistics and analysis of disease risks vs. vaccine risks, the Physicians for Informed Consent (PIC) Measles Disease Information Statement (DIS) and Vaccine Risk Statement (VRS) provide important facts for making an informed risk/benefit calculation for vaccination. Read on for additional information about the risks of measles compared to the risks of the MMR vaccine, with answers to readers' questions about the DIS and VRS.

1. When assessing the risks of measles, why is disease risk sometimes measured using data from various time periods, like the pre-vaccine era (the late 1950s and early 1960s, before the vaccine was introduced), the 1980s, and 1990s?

Pre-vaccine data is necessary to account for the risk of getting measles, as the incidence has been significantly reduced by the mass vaccination program. However, there have been important advancements in health care, measles research, and surveillance of complications from measles since the 1960s. Therefore, information is also derived from more recent data concerning measles cases in U.S. populations.

## 2. Some sources estimate the measles case-fatality rate as 1 in 1,000, but PIC states that the actual case-fatality rate is 1 in 10,000. Why is that?

A pre-vaccination rate of about 1 in 1,000 reported cases has been publicized by public health departments. However, the key word is "reported." Only 10% of cases are reported to public health departments, such as the Centers for Disease Control and Prevention (CDC).

Since nearly 90% of measles cases are not reported to the CDC, the result is a case-fatality rate of 1 in 10,000 for all measles cases. It is important to measure disease risks based on total measles cases, not just the 10% of cases that are reported.

### 3. If not all cases are reported to the CDC, how is it known that only 10% are reported?

Blood tests in samples of the pre-vaccine population showed that nearly everyone contracted measles at some



Being educated about the risks of measles vs. the risks of the MMR vaccine helps to ensure an informed decision about vaccination.

point in their youth. Consequently, on average, there were about as many measles cases annually as there were people being born into the population. Since the size of the pre-vaccine birth cohort was 4 million, there was an average of 4 million measles cases per year. Of these 4 million, only 440,000 were reported.

#### 4. What is the basis for saying all deaths are reported?

U.S. mortality records for measles are based on the cause of death documented in death certificates. Unlike reported measles cases, for which there is evidence of significant underreporting, there is no evidence that a significant number of death certificates are missing or failing to document measles deaths.

### 5. Has the MMR vaccine caused a change in the age distribution of reported measles cases?

Yes. There is evidence that since the measles vaccination program began, there is a disproportionate number of reported measles cases in very young and older individuals compared to the pre-vaccination era.

Before the 1980s, children between 5 and 19 years of age comprised more than 72% of all reported measles cases and less than 3% of reported cases were 20 or older. By 1990, only 35% of reported measles cases were between 5 and 19 years of age, and 17% of reported cases were 20 or older.

Before the mass vaccination program, nearly every child had a mild case of measles by age 15; therefore, older individuals were immune and not susceptible to measles. Also, when infants are born to mothers who have had naturally acquired measles, they are protected from measles via maternal immunity for a longer period of time than those born to vaccinated mothers. Therefore, maternal immunity protected babies for a longer period of time in the early months of life during the pre-vaccine era vs. today.

### 6. For measles, how is the mortality rate different from the case-fatality rate?

Mortality and case fatality are measurements with respect to different groups. Mortality rates are with respect to everyone in the population, regardless of whether they contracted the disease. In contrast, case-fatality rates are with respect to only that subset of the population that actually contracted the disease.

Right before the measles vaccine was introduced, the mortality rate was 0.2 per 100,000 in the population of the U.S., which means 1 person from 500,000 people living in the U.S. died from measles annually. Note that annually, only 2% of people in the U.S. contracted measles; there were only 4 million annual cases out of a population of 200 million.

During this same time period, the case-fatality rate was 1 in 10,000, which means for every 10,000 people who had measles, 1 person died annually.

7. What is the difference between the measles mortality rate of 0.2 per 100,000 in the U.S. population vs. the measles mortality rate of 0.9 per 100,000 children under age 10? Why are these figures (0.2 and 0.9) different?

These figures are looking at different groups. When looking at all ages of individuals in the U.S. population, in 1963 the mortality (or death) rate was 0.2 per 100,000 because there were about 400 measles deaths out of a population of 200 million. In contrast, when looking at children under age 10, the death rate was 0.9 per 100,000 because there were about 360 deaths in children under age 10 out of a population of 40 million children under age 10.

### 8. How many cases of death and encephalitis were there in the pre-vaccine era?

Between 1959 and 1962, annually there were about 400 measles deaths out of 4 million cases (or 1 in 10,000). Because there are about half as many cases of measles encephalitis as there are measles deaths, there were about 200 cases of measles encephalitis (or 1 in 20,000) in the pre-vaccine era.

9. Some sources state that there were 4,000 annual cases of measles encephalitis in the 1960s, yet measles encephalitis actually occurred in 1 in 20,000 cases—a total of 200 cases (4 million/20,000). What is going on?

Measles surveillance from 1985 to 1992 revealed that measles encephalitis occurred in 1 in 1,000 reported cases. Some sources make the mistake of multiplying this ratio by the number of *total* cases in the 1960s, when instead, the ratio should be multiplied by the number of *reported* cases. In addition, some sources do not account for the fact that measles surveillance from 1985 to 1992 also revealed that measles encephalitis occurs half as often as death from measles. Therefore, since there were 400 annual measles deaths in the 1960s, there were about 200 cases of encephalitis out of 4 million total cases (1 in 20,000 cases).

### 10. What is the risk of dying from subacute sclerosing panencephalitis (SSPE) if you contract measles?

The risk of SSPE is between 6 and 22 out of a million measles cases, as cited in the MMR package insert.

### 11. Is the study by Bellini, which estimates the risk of SSPE to be 7–11 cases per 100,000 cases of measles, accurate?

No. Bellini found 12 cases of SSPE between 1989 and 1991 and derived a risk estimate under the assumption that 30% to 50% of all measles cases were reported. These percentages were based on studies of the reporting practices of hospitals and health care providers. However, most measles cases do not require medical attention; therefore, extrapolating the reporting completeness of measles cases that required medical attention to all measles cases is not appropriate.

In contrast, if the 12 cases of SSPE are compared to the 123 measles fatalities between 1989 and 1991, it can be reasonably estimated that there was 1 case of SSPE for every 10 measles deaths. Since the measles case fatality rate is 1 in 10,000, the SSPE risk Bellini found was about 1 in 100,000 (or 10 in a million).

### 12. Why aren't VRS calculations based on all three viruses in the MMR (measles, mumps, and rubella) vaccine when comparing to the risk of measles?

When assessing the disease risk of measles compared to the vaccine, there is no choice but to evaluate against MMR because the measles vaccine alone is no longer available in the U.S.

### 13. What are the risks of dying from measles today in the U.S.?

The risk of dying from measles has not changed since 1963. It is still 1 in 10,000 cases (or 1 in 1,000 reported cases) in the U.S.

### 14. What would happen today if everyone in the U.S. got measles?

For every 8,000 cases of measles, 7,999 cases or 99.99% would fully recover. This is known because in the 1960s, when everyone got measles, 1 in 10,000 cases would die from measles and 1 in 40,000 cases would suffer permanent injury or develop SSPE, a total of 1 in 8,000 cases (1 in 10,000 plus 1 in 40,000).

## 15. Back in the early 1960s, there were hundreds of deaths and permanent injuries from measles. Is PIC proposing that everyone in the U.S. get measles?

No. The goal is to reduce deaths and disabilities, from any cause, as much as possible. The public should be made aware that vaccination is not the only way to prevent death from measles. For example, it has been scientifically confirmed that low levels of vitamin A are associated with measles mortality. Indeed, populations with prevalent vitamin A deficiency are 30–60 times more likely to die from measles. Parents and physicians should consider all the facts that pertain to the children in their care when weighing their options.

## 16. Some possible side effects of the MMR vaccine are included in the Vaccine Risk Statement (VRS). Are there other possible side effects, and if so, where can they be found?

Yes. The MMR package insert contains a longer list of possible side effects.

### 17. How is it known that the MMR vaccine causes febrile seizures in 1 in 640 children?

This finding is derived from results of the most statistically powered safety study ever to measure the association between MMR vaccination and febrile seizures. More than half a million children were evaluated, both vaccinated and unvaccinated, from a Danish population that is relied upon globally to examine vaccine safety. Published in the *Journal of the American Medical Association*, the results showed that seizures from the MMR vaccine occur in about 1 in 640 children up to two weeks following MMR vaccination.

### 18. Some sources say febrile seizures occur less frequently than 1 in 640. Why is that?

There are various studies that look at the association between seizures and the MMR vaccine, however they are weak in their statistical power. The seizure risk of 1 in 640 children is derived from a comprehensive study that examined over half a million children, and included 98,000 unvaccinated kids in the control group. Thus, it is the study with the greatest statistical power available regarding seizures and the MMR vaccine.

## 19. Can epidemiological studies show the MMR vaccine "causes" seizures in some children or only that the MMR vaccine is "associated" with an increased risk of seizures?

MMR vaccination can cause seizures because measles infection can cause seizures. Injecting a live measles virus (that's in the MMR vaccine) into a person introduces the potential for that virus, in combination with various substances in the vaccine, to cause a seizure. In this context, epidemiological studies are not needed to prove causation; rather, they are needed to measure the extent to which MMR causes seizures.

### 20. How many febrile seizures does the MMR vaccine cause in the U.S. annually?

The MMR vaccine causes about 5,700 seizures annually in the U.S. (applying the risk of seizures [1 in 640] to the 3.64 million U.S. children vaccinated with a first dose of MMR every year), as reported in a PIC 2017 Letter to the Editor in the *BMJ*.

## 21. How is it known that 3.64 million U.S. children are vaccinated with a first dose of the MMR vaccine per year?

A birth cohort consists of about 4 million children, and the CDC Pink Book states that vaccine coverage for the MMR vaccine is 91%. Thus, 91% of 4 million is 3.64 million children annually that receive the first dose of MMR.

### 22. Is a febrile seizure from MMR vaccination a medical emergency?

Febrile seizures from measles vaccination often require a medical visit to the emergency department.

#### 23. Some sources say febrile seizures are transient. Can seizures from the MMR vaccine lead to permanent harm?

Yes. Five percent of febrile seizures result in epilepsy, a brain disorder that leads to recurring seizures and permanent harm.

### 24. How many cases of epilepsy does the MMR vaccine cause each year?

About 300 MMR-vaccine seizures (5% of 5,700) will lead to epilepsy annually in the U.S., as explained in the PIC 2017 Letter to the Editor in the *BMJ*.

### 25. Does the Vaccine Adverse Event Reporting System (VAERS) monitor MMR-vaccine seizure rates?

Yes, but not sufficiently. VAERS is a passive reporting system that is significantly limited by underreporting. VAERS receives only 90 annual reports of MMR-vaccine seizures following the first dose—that's only 1.6% of the 5,700 MMR-vaccine seizures that actually occur. Thus, other serious vaccine adverse events from MMR, including permanent neurological harm and death, may similarly be underreported.

### 26. Does measles cause more or less harm than the MMR vaccine?

The answer to this question is not known. In the prevaccine era, measles caused 400 annual cases of death and 100 annual cases of permanent harm; however, most serious measles cases are preventable with adequate levels of vitamin A. In contrast, the MMR vaccine causes 5,700 annual seizures, of which 300 (5%) result in epilepsy; and seizures are only 12% of the serious reactions from the MMR vaccine that are reported to VAERS. Furthermore, the Measles Vaccine Risk Statement (VRS) also shows that studies have not ruled out the possibility of MMR causing permanent harm four times more often than measles causes death.

### 27. What is the importance of examining certain MMR vaccine safety studies from the early 2000s?

Certain studies in the early 2000s were the largest ever conducted that included control groups not vaccinated with MMR. These studies were a response to safety concerns about the MMR vaccine that threatened the mass vaccination program in the late 1990s.

#### 28. The measles mass vaccination program has eliminated endemic measles in the U.S. Isn't this proof that the benefits outweigh the risks?

The available research and data have not proven that the risks of the MMR vaccine are less than the risks of measles, as described in the Measles DIS and VRS.

### 29. Does PIC encourage parents not to vaccinate children with the MMR vaccine?

Physicians for Informed Consent does not provide any personal medical advice. However, PIC does encourage parents to make informed decisions. After reviewing PIC's educational materials, a parent may decide to accept or decline the MMR vaccine, or any vaccine.

For more information about measles and the MMR vaccine, visit physiciansforinformedconsent.org/measles.

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### Feature

## The unofficial vaccine educators: are CDC funded non-profits sufficiently independent?

BMJ 2017; 359 doi: <u>https://doi.org/10.1136/bmj.j5104</u> (Published 07 November 2017) Cite this as: BMJ 2017;359:j5104

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## Re: The unofficial vaccine educators: are CDC funded non-profits sufficiently independent?

#### Dear Editor,

We commend Doshi on citing "insufficient evidence" for a benefit from mandatory influenza vaccination in healthcare workers and exposing conflicts of interest. [1] In the same vein, our organization has found that it has not been proven that the MMR vaccine results in less death or permanent disability than what is expected from measles.[2] The risk of dying or suffering permanent injury from measles in the United States was very small, even before the measles vaccine was introduced in 1963. Therefore, vaccine safety studies must show that the risk of dying or suffering permanent injury from the MMR vaccine is even smaller.

In the late 1950s and early 1960s, right before the measles mass vaccination program was introduced, the chance of dying from measles was 1 in 10,000 or 0.01%.[3] However, the public is generally unaware of this figure as the CDC publishes case-fatality rates based on the number of reported cases only. Since it is estimated that nearly 90% of measles cases are benign and therefore not reported to the CDC, the widely publicized measles case-fatality rate is 10 times higher than what is actually found in the general population.

Furthermore, a large 2004 Danish epidemiological study published in JAMA found that the risk of febrile seizures after MMR vaccination is 1 in 640[4] —a five-fold higher risk of febrile seizure than the risk of seizure from measles.[5] Vestergaard et al. studied the association between MMR and seizures in about 537,000 Danish children 0 to 14 days following MMR vaccination and found 1.56 MMR-related febrile

seizure cases per 1,000 vaccinated children aged 15 to 17 months (95% CI, 1.44 to 1.68). Vestergaard's results are based on 973 febrile seizures within two weeks of MMR vaccination, a robust database containing about 18,000 febrile seizures, and a nonvaccinated control group of about 98,000 children. Applying the 1 in 640 risk of febrile seizure to the 3.64 million U.S. children (91% vaccination rate applied to 4 million children[6]) vaccinated with MMR every year results in about 5,700 annual MMR-related seizures.

Measles surveillance in the 1980s and 1990s revealed that there are 3 to 3.5 times more measles seizures than measles deaths.[5] Therefore, because the measles case-fatality rate is 1 in 10,000, the seizure rate from measles is 3 to 3.5 in 10,000 (mean 1 in 3,100). Although 1.56 MMR-related febrile seizures in 1,000 (about 1 in 640) is a small risk, it is five-fold higher than the 1 in 3,100 risk of seizures from measles.[5] In addition, a significant portion of febrile seizures have permanent sequelae. A large 2007 epidemiological study found that 5% of febrile seizures result in epilepsy.[7]

A query of the Vaccine Adverse Event Reporting System (VAERS) for symptoms involving seizures and convulsions from all measles vaccines (for U.S. children age 6 months to 2 years, between 2011 and 2015) results in about 90 seizure reports per year.[8] This is only 1.6% of the about 5,700 expected MMR-related seizures based on Vestergaard's findings. Other serious vaccine adverse events after MMR, including deaths, may similarly be underreported.

As with mandatory influenza vaccination, there is insufficient evidence that mandatory measles vaccination results in a net public health benefit.

Sincerely, Shira Miller, M.D. President, Physicians for Informed Consent

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3. Physicians for Informed Consent. Measles – Disease Information Statement (DIS). Oct 2017, <u>https://www.physiciansforinformedconsent.org/measles/dis</u>.

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Competing interests: No competing interests

**18 November 2017** Shira Miller Physician Physicians for Informed Consent California, USA <u>picphysicians</u>



### Measles case confirmed in child with MMR vaccine

by KATU News | Friday, February 1st

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VANCOUVER, Wash. - Clark County Health Officials now say they've confirmed 42 cases of measles and the latest confirmed case is in a child who has had one dose of the measles, mumps and rubella vaccine. They are also investigating seven other suspected cases as the outbreak continues to grow.

Those who are infected visited several public locations while contagious.

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Officials say they have not identified any new exposure sites since Thursday.

According to officials, 31 of the measles cases involve kids under 10 years old, ten cases are in youth ages 11 to 18, and one case is someone over 19 years old.

Officials say 37 of those were not immunized, one case is in a person who has had a vaccine, and four cases are not verified to have had the vaccine.

Measles symptoms begin with a mild fever, cough, runny nose and red eyes, followed by a rash.

If you have any further questions about the measles, call your local health department:

- Clark County Public Health: <u>(360) 397-8021 (tel:(360)</u> <u>397-8021)</u>
- Clackamas County Public Health: (503) 655-8411 (tel: (503) 655-8411)
- Multnomah County Public Health: <u>(503) 988-3406 (tel:</u> (503) 988-3406)
- Washington County Public Health: (503) 846-3594 (tel: (503) 846-3594)

Oregon residents can visit the <u>Oregon Health Authority website</u> (https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/VA <u>CCINESIMMUNIZATION/GETTINGIMMUNIZED/Pages/ImmRe</u> <u>cords.aspx</u>) to find out if they're vaccinated.

"Measles can be so contagious that you can be in a room, and if you're susceptible, two hours after someone with measles left, and still get the disease," said Dr. Alan Melnick, the director of public health for Clark County.

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(http://katu.com/news/nation-world/police-woman-raped-child-as-man-held-him-down? utm\_source-taboola&utm\_medium=referrai&utm\_campaign=Internai) (http://katu.com/news/local/snow-storm-delayed-but-2-4-Inches-still-expected-saturday-morning? utm\_source=taboola&utm\_medium=referrai&utm\_campaign=Internai)

Storm Tracker Weather Alert: 2-4 inches expected to fall through Saturday morning



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Intended for healthcare professionals

### News

## Measles: two US outbreaks are blamed on low vaccination rates

BMJ 2019; 364 doi: <u>https://doi.org/10.1136/bmj.I312</u> (Published 21 January 2019) Cite this as: BMJ 2019;364:I312

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## Re: Measles: two US outbreaks are blamed on low vaccination rates. Another perspective

Please allow me to make a few corrections and add context to Ms. Tanne's article. Endemic measles has been eradicated from the US and the whole of the western hemisphere, per the WHO.(1) It does not continually recirculate. But cases are brought into the US, or rarely occur as a clinical response to measles vaccination, (2) multiple times each year. (3) The US averages about 250 reported cases annually.

There have been only 3 deaths from measles in the US since 2000: one in a 75 year old male who was exposed in Israel; one in a 13 year old immunosuppressed male who had received a bone marrow transplant 3 months premortem, who lacked any identified exposure to a measles case; and one in an immunosuppressed woman with multiple comorbidities. Whether any of these deaths was caused by a vaccine strain is unknown, but since vaccine strain measles can be virulent in an immunocompromised host, it is possible. (2)

There are approximately 2500 mumps cases yearly in the US, but no recent mumps-related deaths.(4) There are approximately 10 rubella cases yearly in the US, but since 2012, all rubella cases were infected outside the US. (5)

Thus, there is no evidence that in recent years unvaccinated US children have caused a single death from measles, mumps and rubella. Yet how many column inches, how many hours of TV news have been devoted to scaring the American public about the dire threat of measles? Fear of measles has been the major driver of the campaigns to eliminate vaccine exemptions. Parents of immunocompromised

children have been incited to frenzy about the risks posed to their children by unvaccinated classmates. Yet, when you look closely, the risk is marginal to none.

Even when all eligible children are vaccinated, there will remain those who cannot be vaccinated with live vaccines, and those who fall to achieve immunity from their immunizations. Even after 2 doses, the mumps vaccine is only 86% efficacious. (6) Measles vaccine is 85-95% efficacious after one dose, (7) and 90-98% after two.(8) In US and Canadian measles outbreaks, up to 50% of those developing measles have received two doses of MMR. (8) Thus, there will continue to be disease outbreaks, with or without ending the practice of vaccine exemptions.

During the past 30 years, approximately 89,000 adverse reactions, including about 450 deaths, have been reported to the US Vaccine Adverse Event Reporting System for measles vaccines.

Ms Tanne seems to be singing with a Pharma-led chorus this week, orchestrated with the WHO, BMJ, NY Times and other media outlets. Simultaneously, similar bills have been introduced this month in US state legislatures to end all vaccine exemptions.

But consider: if vaccine exemptions are withheld from children whose families perceive them to be at high risk of an adverse reaction from the MMR, we are likely to experience an inversion in public health: fewer overall viral infections, but more vaccine reactions (and child deaths) then we have now. Public health won't prevail, but Pharma profits will.

- 1. https://www.nbcnews.com/health/health-news/measles-has-been-eliminated-a...
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- 8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3570049/

#### Competing interests: No competing interests

#### 22 January 2019

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