Támogatás zárójelentés

Támogatási azonosító: R18 HS 017045

Elektronikus támogatás a közegészségügy számára - Oltási mellékhatások jelentési rendszere (ESP:VAERS)

Időpontok: 12/01/07 - 09/30/10

Vizsgálati vezető:
Lazarus, Ross, MBBS, MPH, MMed, GDCompSci

Csapattagok:
Michael Klompas, MD, MPH

Előadó szervezet:
Harvard Pilgrim Health Care, Inc.

Projektfelelős:
Steve Bernstein

Benyújtva:
Az Egészségügyi Kutatási és Minőségügyi Ügynökség (AHRQ)
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Absztrakt

Cél: A HIT-tudományos bizonyítékok és bizonyítékokon alapuló eszközök fejlesztése és terjesztése az egészségügyi döntéshozatal javítása érdekében az integrált adat- és tudásmenedzsment alkalmazásával.

Terjedelem: A nemzeti oltási programok biztonságának javítása érdekében egy olyan általánosítható rendszer létrehozása, amely megkönnyíti az oltóanyagokkal kapcsolatos nemkívánatos események észlelését és klinikai bejelentését.

Módszerek: A vizsgálathoz egy nagy, több szakterülettel foglalkozó rendelőben az összes ambuláns ellátást igénybe vevő elektronikus orvosi nyilvántartást használták. Minden oltásban részesülő beteget automatikusan azonosítottak, és a következő 30 napban az egészségügyi diagnosztikai kódokat, laboratóriumi vizsgálatokat és gyógyszerfelírásokat értékelték a nemkívánatos eseményre utaló értékek szempontjából.

Eredmények: A CDC-nél végrehajtott átszervezések és az ebből következő késedelmek a döntéshozatal tekintetében a legjobb erőfeszítések ellenére is kihívást jelentettek az ESP:VAERS teljesítményének randomizált vizsgálatban történő értékelésével kapcsolatos megbeszélések előrehaladásában, valamint az ESP:VAERS teljesítményének a VAERS és a Vaccine Safety Datalink meglévő adataival való összehasonlításában. Előzetes adatokat azonban gyűjtöttek és elemeztek, és ezt a kezdeményezést számos nemzeti szimpóziumon bemutatták.

Kulcsszavak: elektronikus egészségügyi nyilvántartás, védőoltások, nemkívánatos események jelentése

Cél

Ezt a kutatási projektet a vakcinázási programok minőségének javítása érdekében finanszírozták, az orvosok által a nemkívánatos oltási események észlelésének és a nemzeti vakcinajelentési rendszer (VAERS) felé történő jelentésének minőségének javítása révén, a következő célok révén:

1. cél. A szükséges adatelemek azonosítása és rendszerek kifejlesztése a járóbeteg-ellátás elektronikus orvosi nyilvántartásainak a vakcina beadását követő nemkívánatos események nyomon követésére.

2. cél. A klinikusok által jóváhagyott elektronikus jelentések elkészítése és biztonságos benyújtása a nemzeti oltási mellékhatások jelentési rendszeréhez (VAERS).

3. cél. Az ESP:VAERS teljesítményének átfogó értékelése egy randomizált vizsgálatban, valamint a VAERS és a Vaccine Safety Datalink meglévő adataival összehasonlítva.

4. cél. Az 1. és 2. cél keretében kifejlesztett és továbbfejlesztett dokumentációs és alkalmazási szoftverek terjesztése, amelyek más ambuláns ellátórendszerekbe és más EMR-rendszerekbe is átvihetők.

Terjedelem

A lakosság és a szakemberek vakcinázásba vetett bizalma a forgalomba hozatal utáni megbízható felügyeleti rendszerektől függ, amelyek biztosítják, hogy a ritka és váratlan mellékhatásokat gyorsan azonosítják. A projekt célja az oltási programok minőségének javítása az orvosok által a nemkívánatos oltási események észlelésének és a nemzeti oltási mellékhatások jelentési rendszere (VAERS) felé történő jelentésének minőségének javításával. Ez a projekt az Elektronikus közegészségügyi támogatás (ESP) projekt kiterjesztéseként szolgál, amely egy olyan automatizált rendszer, amely az elektronikus egészségügyi nyilvántartás (EHR) adatait használja bizonyos betegségek eseteinek felderítésére és biztonságos jelentésére a helyi közegészségügyi hatóságnak. Az ESP kész platformot biztosít a klinikai, laboratóriumi, vényköteles és demográfiai adatok automatikus átalakítására szinte bármilyen EHR-rendszerből egy teljesen független szerveren lévő adatbázis-táblákba, amely fizikailag ugyanolyan logikai és fizikai biztonsággal van ellátva, mint maga az EHR-adatok. Az ESP:VAERS projekt kritériumokat és algoritmusokat dolgozott ki a védőoltásokkal kapcsolatos fontos nemkívánatos események azonosítására az ambuláns egészségügyi EHR-adatokban, és kísérleteket tett az elektronikus VAERS-jelentések formázására és biztonságos elküldésére közvetlenül a Betegségellenőrzési és Megelőzési Központoknak (CDC).

A betegadatok az Epic System Egészségügyi Információs Technológia Tanúsító Bizottságának tanúsított EpicCare rendszeréből álltak rendelkezésre az Atrius Health, egy nagy,

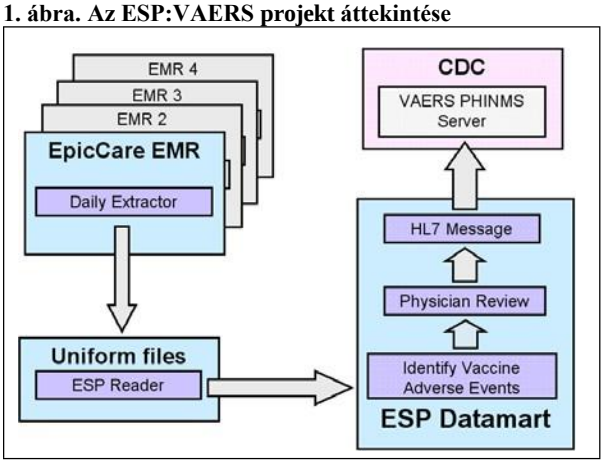
több mint 35 létesítményt magában foglaló, multispeciális csoportos gyakorlaton belüli összes ambuláns ellátási találkozásnál. Minden oltásban részesülő beteget automatikusan azonosítottak, és a következő 30 napban az egészségügyi diagnosztikai kódjaikat, laboratóriumi vizsgálataikat és gyógyszerfelírásaikat értékelték az értékek tekintetében amely nemkívánatos oltási eseményre utal. Ha lehetséges nemkívánatos eseményt észleltek, azt rögzítették, és a megfelelő klinikust elektronikus úton értesítették.

A klinikusok kosárba küldött üzenetküldését úgy tervezték, hogy egy előzetesen kitöltött jelentés előnézetét nyújtsa az EHR-ből származó, a betegre vonatkozó információkkal, beleértve a vakcina típusát, tételszámát és a lehetséges mellékhatást, hogy klinikai döntésük alapján meg tudják ítélni, hogy kívánnak-e jelentést küldeni a VAERS-nek. A klinikusoknak ezután lehetőségük lenne arra, hogy szabadszöveges megjegyzéseket fűzzenek az előre kitöltött VAERS-jelentésekhez, vagy dokumentálják a jelentés elküldését mellőző döntésüket. A CDC Közegészségügyi Információs Hálózati Üzenetküldő Rendszer (PHIN-MS) szoftverét telepítették a létesítményekbe, hogy a jóváhagyott jelentéseket biztonságosan, elektronikus üzenetek formájában, interoperábilis egészségügyi adatcsere-formátumban, a HL7 (Health Level 7) segítségével továbbítani lehessen a VAERS-nek.

Módszerek

Az 1. cél: a *szükséges adatelemek azonosítása és olyan rendszerek kifejlesztése, amelyek a járóbeteg-ellátás elektronikus orvosi nyilvántartását figyelemmel kísérik a vakcina beadását követő nemkívánatos események tekintetében*, valamint a 2. cél: a *klinikusok által jóváhagyott elektronikus jelentések elkészítése és biztonságos benyújtása a nemzeti vakcinák nemkívánatos eseményeit bejelentő rendszerhez (VAERS), az* alábbi adatáramlás kialakítása volt a cél az első két cél támogatása érdekében:

1. ábra. Az ESP:VAERS projekt áttekintése



A bal oldalon a meglévő és működő ESP-elemek, a jobb oldalon pedig az 1. és 2. célkitűzés látható. ESP: A VAERS minden beoltott beteget megjelöl, és prospektív módon összegyűjti a beteg diagnosztikai kódjait, laboratóriumi vizsgálatokat, allergialistákat, életjeleket és

gyógyszerfelírásokat. Az 1. cél egyik fő összetevője az *AE-kritériumok kidolgozása* volt*, hogy ezeket a paramétereket olyan új vagy abnormális értékek szempontjából értékeljék, amelyek mellékhatásra utalhatnak.* Jelentési protokollt és megfelelő algoritmusokat dolgoztak ki a potenciális mellékhatás esetek diagnosztikai kódok segítségével történő felderítésére, és módszereket teszteltek a mellékhatásra utaló receptek vagy rendellenes laboratóriumi értékek azonosítására. Ezeket az algoritmusokat úgy tervezték, hogy mind a várt, mind a váratlan mellékhatásokat felkutassák.

Ezt a jelentéstételi protokollt mind a belső, mind a külső partnerek jóváhagyták. Kezdetben egy dokumentumtervezetet készítettünk, amely leírja az oltás utáni események széles csoportjaira vonatkozó elemeket, algoritmusokat, az oltás utáni érdeklődési intervallumot és intézkedéseket, beleértve az azonnal és késedelem nélkül jelentendő eseményeket (mint például az oltást követő akut anafilaxiás reakció), a soha nem jelentendő eseményeket (mint például az oltást követő rutinellenőrzés) és azokat, amelyeket a kezelőorvos belátása szerint és kiegészítő információkkal kell jelenteni egy visszajelzési mechanizmuson keresztül. A tervezetet ezután széles körben terjesztettük, hogy a CDC illetékes munkatársai és az Atrius klinikai munkatársai véleményezhessék azt, mint kezdeti/munkavázlatot. A CDC Brighton Collaboration belső összekötője által végzett felülvizsgálaton kívül ez a protokoll a CDC klinikai immunizációs biztonsági értékelési hálózatán (CISA) keresztül is kapott felülvizsgálatot és észrevételeket.

A 2. célkitűzés célja az *ESP:VAERS HL7 üzenetkódok kifejlesztése* volt*,* hogy a *PHIN-MS-en keresztül biztonságos továbbítást biztosítson a CDC-nek.* A CDC által a projekthez megbízott tanácsadóknak, a Constellának küldendő elektronikus üzenet elemeit leíró HL7-specifikációt végrehajtották. Szintetikus és valós tesztadatokat generáltak és továbbítottak a Harvard és a Constella között. A nem orvosok által jóváhagyott jelentések valós adattovábbítása a CDC-nek azonban nem kezdődhetett meg, mivel a projekt végére a CDC még nem válaszolt az e tevékenységre vonatkozó többszöri megkeresésre.

A 3. célkitűzés célja az *ESP:VAERS teljesítményének átfogó értékelése* volt *egy randomizált vizsgálatban, valamint a VAERS és a Vaccine Safety Datalink meglévő adataival összehasonlítva.*

Eredetileg úgy terveztük, hogy a rendszert úgy értékeljük, hogy összehasonlítjuk a nemkívánatos események megállapításait a Vaccine Safety Datalink projektben - a CDC Immunizációs Biztonsági Hivatala és nyolc nagy, irányított ellátó szervezet együttműködésében - szereplő eredményekkel. Egy randomizált kísérlet révén azt a hipotézist is teszteltük volna, hogy a biztonságos, számítógéppel támogatott, klinikus által jóváhagyott, nemkívánatos események észlelésének és az automatikus elektronikus jelentésnek a kombinációja jelentősen növeli az orvos által jóváhagyott, a VAERS-hez küldött esetjelentések számát, teljességét, érvényességét és időszerűségét a meglévő spontán jelentési rendszerhez képest; azonban a CDC-nél történt átszervezések és a döntéshozatal szempontjából ebből következő késedelmek miatt nem lehetett előrehaladni az ESP értékelésével kapcsolatos megbeszélésekkel:VAERS teljesítményének randomizált vizsgálatban történő megvitatása, valamint az ESP:VAERS teljesítményének összehasonlítása a VAERS és a Vaccine Safety Datalink meglévő adataival. Ezért az e konkrét célkitűzéshez tartozó összetevők nem valósultak meg.

4. cél Sikeresen befejeződött *az 1. és 2. cél keretében kifejlesztett és továbbfejlesztett dokumentációs és alkalmazási szoftverek terjesztése, amelyek más ambuláns ellátórendszerekbe és más EMR-rendszerekbe is átvihetők.* A működő forráskód jóváhagyott nyílt forráskódú licenc alapján megosztható. Az ESP:VAERS forráskódja az ESP forráskódjának terjesztése részeként áll rendelkezésre. Az LGPL, egy kereskedelmi felhasználással kompatibilis nyílt forráskódú licenc alatt áll. Az ESP:VAERS kódot, a HL7 és egyéb specifikációkat és dokumentációt

hozzáadtuk a meglévő ESP webes dokumentációhoz és a disztribúciós forrásközponthoz http://esphealth.org, pontosabban a Subversion tárolóhoz, amely a következő címen érhető el: http://esphealth.org/trac/ESP/wiki/ESPVAERS.

Eredmények

Az előzetes adatokat 2006 júniusa és 2009 októbere között gyűjtötték 715 000 betegről, és 1,4 millió adagot (45 különböző vakcinából) adtak be 376 452 személynek. Ezekből az adagokból 35 570 lehetséges reakciót (az oltások 2,6%-a) azonosítottak. Ez átlagosan 890 lehetséges eseményt jelent, ami klinikusonként átlagosan 1,3 eseményt jelent havonta. Ezeket az adatokat a 2009-es AMIA-konferencián mutatták be.

Ezen túlmenően az ESP:VAERS kutatói részt vettek egy panelbeszélgetésen, amely a klinikusok, az elektronikus egészségügyi nyilvántartások (EHR) szállítói, a gyógyszeripar és az FDA nézőpontját vizsgálta a proaktív, automatizált mellékhatás-jelentési rendszerekkel kapcsolatban.

A gyógyszerek és vakcinák okozta mellékhatások gyakoriak, de nem jelentik őket eléggé. Bár az ambuláns betegek 25%-ánál fordul elő gyógyszeres mellékhatás, az összes gyógyszeres mellékhatás kevesebb mint 0,3%-át, a súlyos események 1-13%-át jelentik az Élelmiszer- és Gyógyszerügyi Hivatalnak (FDA).
Hasonlóképpen, a vakcinák mellékhatásainak kevesebb mint 1%-át jelentik. Az alacsony jelentési arányok megakadályozzák vagy lassítják a közegészségügyet veszélyeztető "problémás" gyógyszerek és vakcinák azonosítását. A gyógyszerek és vakcinák mellékhatásaira vonatkozó új felügyeleti módszerekre van szükség. A jelentéstétel akadályai közé tartozik a klinikusok tájékozottságának hiánya, a bizonytalanság azzal kapcsolatban, hogy mikor és mit kell jelenteni, valamint a jelentéssel járó terhek: a jelentés nem része a klinikusok szokásos munkafolyamatának, időigényes és párhuzamos. Az EHR-ekbe és más információs rendszerekbe ágyazott proaktív, spontán, automatizált mellékhatásjelentés felgyorsíthatja az új gyógyszerekkel kapcsolatos problémák azonosítását és a régebbi gyógyszerek kockázatainak gondosabb számszerűsítését.

Sajnos soha nem volt lehetőség a rendszer teljesítményértékelésének elvégzésére, mivel a szükséges CDC-kapcsolatok már nem álltak rendelkezésre, és az adatok átvételéért felelős CDC-tanácsadók már nem reagáltak a tesztelés és értékelés folytatására irányuló többszöri kérésünkre.

Az AHRQ kiemelt népességcsoportok bevonása

Projektünk középpontjában az Atrius Health (korábban HealthOne) szolgáltatói és betegközösség állt. Ez a közösség számos AHRQ-felvételi populációt szolgál ki, különösen az alacsony jövedelmű és kisebbségi populációkat, elsősorban városi környezetben.

Az Atruis jelenleg mintegy 700 orvost foglalkoztat, akik több mint 18 irodában több mint 500.000 beteget szolgálnak ki a bostoni nagyváros területén. Az Atruis orvosainak többsége alapellátó belgyógyász vagy gyermekorvos, de a hálózatban minden fontosabb szakterület orvosai megtalálhatók.

Az Atruis által ellátott teljes felnőtt és gyermekpopuláció bekerült a mellékhatás-felügyeleti rendszerünkbe (ESP:VAERS). Az Atruis a betegek teljes spektrumát szolgálja ki, amely tükrözi Kelet-Massachusetts széles körű sokszínűségét. Egy nemrégiben végzett elemzés szerint az

Atruis által ellátott lakosság 56%-a nő, 16,6%-a afroamerikai, 4%-a spanyolajkú. A felnőtt lakosság körében a 2-es típusú cukorbetegség előfordulási aránya 5,7%. Az Atruis lakosságának körülbelül egynegyede 18 év alatti.

Kiadványok és termékek listája

ESP:VAERS [a forráskód elérhető az ESP forráskód terjesztésének részeként]. Licencelve a GNU Lesser General Public License (LGPL), egy nyílt forráskódú licenc alatt, amely kompatibilis a kereskedelmi felhasználással. Szabadon hozzáférhető egy jóváhagyott nyílt forráskódú licenc alapján a következő címen: http://esphealth.org.

Lazarus, R, Klompas M, Hou X, Campion FX, Dunn J, Platt R. Az oltást követő nemkívánatos események automatizált elektronikus észlelése és jelentése: ESP: VAERS. A CDC Vaccine Safety Datalink (VSD) éves találkozója.
Atlanta, GA; 2008. április.

Lazarus R, Klompas M Automatizált vakcina mellékhatások észlelése és jelentése elektronikus orvosi nyilvántartásokból. A CDC közegészségügyi informatikai hálózat (PHIN) konferenciája 2008. augusztus 27.

Klompas M, Lazarus R ESP: VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 november 17.

Lazarus R, Klompas M, Kruskal B, Platt R Az ESP:VAERS által azonosított láz időbeli mintázatai az immunizálást követő lázzal kapcsolatban az ambuláns ellátási adatokban Előadás az American Medical Informatics Association éves szimpóziumán; 2009. november 14-18.: San Francisco, CA.

Linder J, Klompas M, Cass B, et al. Spontán elektronikus mellékhatás-jelentés: EHR-szolgáltatók, biofarmácia és az FDA. Előadás az Amerikai Orvosi Informatikai Társaság konferenciáján.
Éves szimpózium; 2009. november 14-18.: San Francisco, Kalifornia.

Kutatási **cikkISSN 2639-**

Mikrobiológia & Fertőző betegségek

9458

COVID-19 RNS-alapú vakcinák és a prionbetegség kockázata

J. Bart Classen, MD*

Classen Immunotherapies, Inc., 3637 Rockdale Road, Manchester, MD 21102, E-mail: classen@vaccines.net.

***Levelezés:**
J. Bart Classen, MD, Classen Immunotherapies, Inc., 3637 Rockdale Road, Manchester, MD 21102, Tel: 410-377-8526.

Megérkezett: Elfogadva: 2020. december 27: január 18.

Idézet: Classen JB. COVID-19 RNS-alapú vakcinák és a prionbetegség kockázata. Microbiol Infect Dis. 2021; 5(1): 1-3.

ABSZTRAKT

Az új vakcinatechnológia fejlesztése a múltban problémákkal járt. A jelenlegi RNS-alapú SARS-CoV-2 vakcinákat az Egyesült Államokban sürgősségi rendelettel, kiterjedt hosszú távú biztonságossági vizsgálatok nélkül hagyták jóvá. Ebben a tanulmányban a Pfizer COVID-19 vakcinát vizsgálták a tekintetben, hogy a vakcinát kapókban prionalapú betegséget idézhet-e elő. A vakcina RNS-szekvenciáját, valamint a tüskefehérje célinterakcióját elemezték, hogy képes-e az intracelluláris RNS-kötő fehérjéket, a TAR DNS-kötő fehérjét (TDP-43) és a Fused in Sarcoma (FUS) fehérjét a patológiás prionkonformációjukba alakítani. Az eredmények azt mutatják, hogy a vakcina RNS olyan specifikus szekvenciákkal rendelkezik, amelyek a TDP-43 és a FUS patológiás prionkonformációba történő összehajlását indukálhatják. A jelenlegi elemzés során összesen tizenhat UG tandem ismétlődést (ΨGΨG) azonosítottak, és további UG (ΨG) gazdag szekvenciákat azonosítottak. Két GGΨA szekvenciát találtak. Lehetséges, hogy potenciális G kvadruplex szekvenciák is jelen vannak, de ezek ellenőrzéséhez kifinomultabb számítógépes programra van szükség. Továbbá a vakcina RNS fordításával létrehozott spike fehérje az angiotenzin konvertáló enzim 2 (ACE2), egy cinket tartalmazó enzimhez kötődik. Ez a kölcsönhatás növelheti az intracelluláris cink mennyiségét. Kimutatták, hogy a cinkionok a TDP-43 kóros prionkonfigurációvá alakulását okozzák. A TDP-43 és a FUS patológiás prionkonfigurációba történő összehajlása ismert az ALS, a frontális temporális lebeny degeneráció, az Alzheimer-kór és más neurológiai degeneratív betegségek okozója. A mellékelt megállapítás, valamint a további lehetséges kockázatok miatt a

Kulcsszavak
COVID-19, vakcinák, cukorbetegség, immunitás.

Bevezetés
A vakcinákról kiderült, hogy számos krónikus, később kialakuló mellékhatást okoznak. Egyes mellékhatások, mint például az 1-es típusú cukorbetegség, csak 3-4 évvel a vakcina beadása után jelentkezhetnek [1]. Az 1-es típusú cukorbetegség esetében a nemkívánatos események gyakorisága meghaladhatja a súlyos fertőző betegségek gyakoriságát, amelyek megelőzésére a vakcinát tervezték. Tekintettel arra, hogy az 1-es típusú cukorbetegség csak egy a sok immunmediált betegség közül, amelyet vakcinák okozhatnak, a krónikus, később jelentkező mellékhatások komoly közegészségügyi problémát jelentenek.

Az új vakcinatechnológia megjelenése a vakcina mellékhatásainak új lehetséges mechanizmusait hozza létre. Például az első elölt gyermekbénulás elleni vakcina valójában gyermekbénulást okozott a befogadókban, mivel a felfejlesztett gyártási eljárás nem ölte meg hatékonyan a a gyermekbénulás vírusát, mielőtt beadnák a betegeknek. Az RNS-alapú vakcinák különleges kockázatot jelentenek a specifikus mellékhatások kiváltásában. Az egyik ilyen lehetséges mellékhatás a prion alapú betegségek, amelyeket a belső fehérjék aktiválása okoz prionok kialakulásával. Rengeteg ismeretet publikáltak az RNS-kötő fehérjék egy osztályáról, amelyekről kimutatták, hogy részt vesznek számos neurológiai betegség, többek között az Alzheimer-kór és az ALS kiváltásában. A TDP-43 és a FUS e fehérjék közül a legjobban tanulmányozottak közé tartoznak [2].

A Pfizer RNS-alapú COVID-19 vakcináját az amerikai FDA sürgősségi felhasználási engedély alapján, hosszú távú biztonsági adatok nélkül hagyta jóvá. A vakcina biztonságosságával kapcsolatos aggályok miatt vizsgálatot végeztek annak megállapítására, hogy a vakcina esetleg prionalapú betegséget idézhet-e elő.

Módszerek
A Pfizer COVID-19 elleni RNS-alapú vakcináját a következőkre értékelték
a TDP-43 és vagy a FUS prionalapúvá alakításának lehetősége.

betegséget okozó állapotok. A vakcina RNS-ét olyan szekvenciák jelenlétére vizsgálták, amelyek aktiválhatják a TDP-43 és a FUS vírusokat. Az átírt tüskefehérje és a célpontja közötti kölcsönhatást elemezték, hogy megállapítsák, ez a hatás aktiválhatja-e a TDP-43-at és a FUS-t is.

Eredmények
A Pfizer COVID-19 elleni vakcinájának elemzése két lehetséges kockázati tényezőt azonosított a prionbetegség emberekben való előidézésére. A vakcinában lévő RNS-szekvencia [3] olyan szekvenciákat tartalmaz, amelyekről feltételezhető, hogy a TDP-43 és a FUS prionalapú konformációban való aggregálódását idézik elő, ami a gyakori neurodegeratív betegségek kialakulásához vezet. Kimutatták, hogy a GGUA [4], az UG gazdag szekvenciák [5], az UG tandem ismétlődések [6] és a G kvadruplex szekvenciák [7] RNS-szekvenciák fokozott affinitással kötődnek a TDP-43-hoz és/vagy a FUS-hoz, és a TDP-43 vagy a FUS a citoplazmában kóros konfigurációba kerülhet. A jelenlegi elemzés során összesen tizenhat UG tandem ismétlődést (ΨGΨG) azonosítottak, és további UG (ΨG) gazdag szekvenciákat azonosítottak. Két GGΨA szekvenciát találtak. A G kvadruplex szekvenciák valószínűleg jelen vannak, de ezek ellenőrzéséhez kifinomult számítógépes programokra van szükség.

A vakcina által kódolt spike fehérje az angiotenzin konvertáló enzim 2-t (ACE2), egy cinkmolekulákat tartalmazó enzimet köt meg [8]. A spike fehérje ACE2-hez való kötődése képes felszabadítani a cinkmolekulát, egy iont, amely a TDP-43 kóros prion átalakulását okozza [9].

Megbeszélés
Van egy régi mondás az orvostudományban, miszerint "a gyógymód rosszabb lehet, mint a betegség". Ez a mondás a vakcinákra is alkalmazható. A jelen tanulmányban az az aggodalom merül fel, hogy az RNS-alapú COVID vakcinák több betegséget okozhatnak, mint a COVID-19 járvány. Ez a tanulmány egy új, potenciális mellékhatási mechanizmusra összpontosít, amely prionbetegséget okoz, amely még gyakoribb és gyengítőbb lehet, mint az a vírusfertőzés, amelyet a vakcina megelőzni hivatott. Bár ez a tanulmány egy lehetséges mellékhatásra összpontosít, az alábbiakban tárgyaltak szerint több más lehetséges halálos kimenetelű mellékhatás is létezik.

Az elmúlt két évtizedben egyes tudósok körében felmerült az az aggodalom, hogy a prionokat biofegyverként lehetne felhasználni. Újabban az az aggodalom is felmerült, hogy a mindenütt jelenlévő intracelluláris molekulák aktiválódhatnak, és prionbetegséget okozhatnak, beleértve az Alzheimer-kórt, az ALS-t és más neurodegeneratív betegségeket. Ez az aggodalom abból adódik, hogy visszaélhetnek a kutatási adatokkal, amelyek arra vonatkoznak, hogy bizonyos RNS-kötő fehérjék, mint például a TDP-43, a FUS és mások, milyen mechanizmusok révén aktiválódhatnak a betegséget okozó prionok kialakulásához. Az a tény, hogy ezt a kutatást, amelyet biológiai fegyverek kifejlesztésére lehet felhasználni, magánszervezetek finanszírozzák, köztük a Bill és Melinda Gates Alapítvány és az Ellison Medical Foundation.
[2] nemzeti/nemzetközi felügyelet nélkül szintén aggodalomra ad okot. A múltban például tilos volt az atombombák építésével kapcsolatos információk közzététele.

A közzétett adatok azt mutatják, hogy számos különböző tényező járulhat hozzá bizonyos RNS-kötő fehérjék, köztük a TDP-43, a FUS és a rokon molekulák kóros állapotba kerüléséhez. Ezek az RNS-kötő fehérjék számos funkcióval rendelkeznek, és mind a sejtmagban, mind a citoplazmában megtalálhatók. Ezek a kötőfehérjék olyan aminosav-régiókkal, kötőmotívumokkal rendelkeznek, amelyek specifikus RNS-szekvenciákat kötnek meg. Bizonyos RNS-szekvenciákhoz való kötődés, amikor a fehérjék a citoplazmában vannak, feltehetően a molekulák bizonyos módon történő összehajlását okozza, ami kóros

aggregációhoz és prionképződéshez vezet a citoplazmában [2]. A jelenlegi elemzés szerint a Pfizer RNS-alapú COVID-19 vakcinája számos ilyen RNS-szekvenciát tartalmaz, amelyekről kimutatták, hogy nagy affinitással rendelkeznek a TDP-43 vagy a FUS iránt, és képesek krónikus degeneratív neurológiai betegségek kiváltására.

A TDP-43 RNS-felismerő motívumához való cinkkötés egy másik mechanizmus, amely az amiloidszerű aggregációk kialakulásához vezet [9]. A vakcina RNS-szekvenciája által kódolt vírus spike fehérje megköti a cinkmolekulákat tartalmazó ACE2 enzimet [8]. Ez a kölcsönhatás potenciálisan megnövelheti az intracelluláris cinkszintet, ami prionbetegséghez vezet. A kezdeti kötődés a vakcina által transzfektált sejt felszínén lévő spike-fehérje és a szomszédos sejt felszínén lévő ACE2 között történhet. A keletkező komplex internalizálódhat. Alternatív megoldásként a kölcsönhatás kezdetben az ACE2-t előállító és a vakcina spike-fehérjét kódoló RNS-sel transzfektált sejt citoplazmájában is létrejöhet. A kölcsönhatás meglehetősen aggasztó, tekintve, hogy a COVID-19-et okozó vírus, a SARS-CoV-2 biológiai fegyver [10,11], és lehetséges, hogy a vírus spike fehérjét úgy tervezték, hogy prionbetegséget okozzon.

Egy másik kapcsolódó aggodalomra ad okot, hogy a Pfizer vakcina egy egyedülálló RNS-nukleozidot, az 1-metil-3'-pszeudouridil (Ψ) nukleozidot használja. Az FDA tájékoztató dokumentumai szerint ezt a nukleozidot azért választották, hogy csökkentse a veleszületett immunrendszer aktiválódását [12]. Az ezt a nukleozidot tartalmazó RNS-molekulák kötődése kétségtelenül megváltozik [13]. Sajnos a TDP-43-ra, a FUS-ra és más RNS-kötő fehérjékre gyakorolt hatást nem publikálták. Ennek a nukleozidnak a vakcinában való alkalmazása potenciálisan fokozhatja a TDP-43 és a FUS toxikus konfigurációjának kialakítására képes RNS-szekvenciák kötődési affinitását.

A COVID-19 elleni új RNS-alapú vakcinák számos egyéb lehetséges mellékhatást is kiválthatnak. A vakcina egy új molekulát, a spike fehérjét helyezi a gazdasejtek felszínére/felületére. Ez a spike fehérje egy másik, esetleg új fertőző ágens potenciális receptora. Ha azoknak van igazuk, akik azt állítják, hogy a COVID-19 valójában biofegyver, akkor egy második, potenciálisan veszélyesebb vírus szabadulhat fel, amely a vakcinát befogadók gazdasejtjein található spike proteinhez kötődik. A nyilvánosság számára nem állnak rendelkezésre olyan adatok, amelyek információt szolgáltatnának arról, hogy a vakcina RNS mennyi ideig transzlálódik a vakcina befogadójában, és a transzláció után mennyi ideig lesz jelen a spike fehérje a befogadó sejtjeiben. Az in vivo expresszióra vonatkozó ilyen vizsgálatok összetettek és nagy kihívást jelentenek. A genetikai sokféleség megvédi a fajokat a fertőző ágensek által okozott tömeges veszteségektől. Egy egyedet elpusztíthat egy vírus, míg egy másiknak lehet, hogy ugyanannak a vírusnak nincsenek betegségei. Azáltal, hogy egy populációban mindenki sejtjén azonos receptor, a spike fehérje található, eltűnik a genetikai sokféleség legalább egy potenciális receptor esetében. A populációban mindenki potenciálisan fogékonnyá válik az azonos fertőző ágenssel való kötődésre.

Az autoimmunitás és az ezzel ellentétes állapot, a metabolikus szindróma jól ismert, vakcinák által okozott mellékhatások [14]. A COVID-19 fertőzéseket autoantitestek és autoimmun betegségek indukciójával hozzák összefüggésbe [15,16], így több mint valószínű, hogy egy vakcina ugyanezt okozhatja. Egy szerző úgy találta, hogy a tüskefehérje által kódolt aminosav-szekvenciák azonosak az emberi fehérjékben, többek között a központi idegrendszerben található fehérjékben található szekvenciákkal [17]. Az autoimmunitást epitópterjedés is kiválthatja, amikor egy idegen antigént, mint például a spike fehérjét, egy olyan antigénprezentáló sejt mutatja be, amelynek MHC-molekuláihoz önmolekulák is kapcsolódnak.

Végezetül, a területen dolgozók további bizonyítékokat tettek közzé annak alátámasztására, hogy a COVID-19 vakcinák potenciálisan prionbetegséget idézhetnek elő. A szerzők [18] a COVID-19 tüskefehérjében olyan prionnal rokon szekvenciákat találtak, amelyek a rokon koronavírusokban nem fordultak elő. Mások [19] beszámoltak egy prionbetegség, a Creutzfeldt-Jakob-kór esetéről, amely kezdetben egy COVID-19 vírussal fertőzött férfinél jelentkezett.

Sokan felvetették azt a figyelmeztetést, hogy a COVID-19 jelenlegi járványa valójában egy olyan biofegyver-támadás eredménye, amelyet részben az Egyesült Államok kormányának egyes tagjai szabadítottak ki [10,11]. Egy ilyen elmélet nem túlzás, tekintve, hogy a 2001-es amerikai lépfene-támadás Fort Detrickből, az amerikai hadsereg biofegyverekkel foglalkozó létesítményéből indult. Mivel az FBI lépfene elleni nyomozását az ügyet vezető FBI-ügynök tanácsa ellenére lezárták, valószínű, hogy az összeesküvők még mindig az amerikai kormányban dolgoznak. Egy ilyen forgatókönyv szerint a biofegyveres támadás megállításának elsődleges célja az összeesküvők elfogása kell, hogy legyen, különben a támadások soha nem fognak megszűnni. Az új RNS-technológiát alkalmazó vakcina jóváhagyása széles körű tesztelés nélkül rendkívül veszélyes. A vakcina lehet biofegyver, és még az eredeti fertőzésnél is veszélyesebb lehet.

Hivatkozások

1. Classen JB, Classen DC. A Hemophilus influenza B (HiB) immunizálás után három évvel előforduló inzulinfüggő cukorbetegség (IDDM) eseteinek csoportosulásai alátámasztják az immunizálás és az IDDM közötti okozati összefüggést. Autoimmunitás. 2002; 35: 247-253.
2. King OD, Gitler AD, Shorter J. A jéghegy csúcsa: RNS-kötő fehérjék prionszerű doménekkel a neurodegeneratív betegségekben. Brain Res. 2012; 1462: 61-80.
3. WHO, Nemzetközi nem védett nevek program: 11889. 9/2020.
4. Kapeli K, Pratt GA, Vu AQ, et al. Distinct and shared functions

a TDP-43, a FUS és a TAF15 ALS-hez kapcsolódó fehérjék multiszisztémás elemzésekkel feltártak. Nature Communications. 2016; 7: 12143.

5. Kuo P, Chiang C, Wang Y, et al. A TDP- 43 RRM1-DNS komplex kristályszerkezete feltárja az UG- és TG-gazdag nukleinsavak specifikus felismerését. Nucleic Acids Research. 2014; 42: 4712-4722.
6. Tollervey JR, Curk T, Rogelj B, et al. A TDP-43 RNS-célpontjainak és pozíciófüggő splicing-szabályozásának jellemzése; a neurodegeneratív betegségek következményei. Nat Neurosci. 2011; 14: 452-458.
7. Imperatore JA, McAninch DS, Valdez-Sinon AN, et al. A FUS felismeri a neuronális mRNS-ek G kvadruplex struktúráit. Frontiers in Molecular Biosciences. 2020; 7: 6.
8. Shang J, Ye G, Shi K, et al. A SARS-CoV-2 receptorfelismerésének strukturális alapja. Nature. 2020; 581: 221-225.
9. Garnier C, Devred F, Byrne D, et al. A TDP-43 RNS-felismerő motívumához kötődő cink amiloid-szerű aggregátumok képződését indukálja. Sci Rep. 2017; 7: 6812.
10. Classen JB. COVID-19, MMR-vakcina és biológiai fegyverek. Diabetes & its Complications.2020; 4: 1-8.
11. Classen JB. Bizonyítékok, amelyek alátámasztják azt a hipotézist, hogy az E-vaping akut tüdőkárosodás (EVALI) 2019-es járványát részben a COVID-19 okozta. Diabetes & Complications. 2020; 4: 1-2.
12. Pfizer-Biotech: (BNT162, PF-07302048), Vakcinák és kapcsolódó biológiai termékek tanácsadó bizottságának tájékoztató dokumentuma. Az ülés időpontja: 2020. december 10.
13. Roundtree IA, Evans ME, Pan, et al. Dynamic RNS modifications in gene expression regulation. Cell. 2017; 169: 1187-1200.
14. Classen JB. A Vaccine Induced Immune Overload and the Resulting Epidemics of Type 1 Diabetes and Metabolic Syndrome, Emphasis on Explaished the Recent Accelerations in the Risk of Prediabetes and other Immune Mediated Diseases. J Mol Genet Med. 2014; S1: 025.
15. Amiral J. A COVID-19 kiválthat-e hosszan tartó tünetekkel és késleltetett szövődményekkel járó autoimmun betegséget? Ann Clin Immunol Microbiol. 2020; 2: 1014.
16. Wang EY, Mao T, Klein J, et al. Diverse functional autoantibodies in patients with COVID-19. medRxiv preprint. 2020.
17. Lyons-Weiler J. A patogén priming valószínűleg hozzájárul a COVID-19 súlyos és kritikus megbetegedéséhez és halálozásához az autoimmunitáson keresztül. Journal of Translational Autoimmunity. 2020; 3: 100051.
18. Tetz G, Tetz V. SARS-CoV-2 prionszerű domének a tüskékben. fehérjék nagyobb affinitást biztosítanak az ACE2-hez. Előnyomtatás. 2020.
19. Young MJ, O'Hare M, Matiello M, et al. Creutzfeldt-Jakob-kór egy COVID-19-es férfinál: SARS-CoV-2 által felgyorsított idegdegeneráció? Agy, viselkedés és immunitás. 2020; 89: 601-603.

Az úgynevezett "eredeti antigén bűn" [Lásd az alábbi 4. ábrát]

Használjunk egy példát az "eredeti antigén bűn" magyarázatára.

- Amikor egy személy kórokozótípusnak van kitéve, az immunrendszer egy nagyon specifikus IgG antitest felszabadulásával válaszol, amely az adott első kórokozó variáns ellen képződik.

- Amikor később a kórokozó valamely variánsának vannak kitéve, a B-sejtek "emlékeznek" az első varíiáns expozícióra, még akkor is, ha az sok évvel ezelőtt történt.

- A B-sejtek "memória-antitesteket" termelnek, nem pedig az adott variáns elleni antitesteket. Ezek az antitestek nem megfelelőek, és nem semlegesítő, nem kötődő antitesteknek nevezik őket.

- Nem védekeznek az új "betolakodó" ellen, hanem inkább fokozzák a fertőzést. A személy nagyon megbetegedhet az antitestfüggő fokozódásnak (ADE) nevezett jelenség révén. Az ADE tartós gyulladást, limfopéniát és néha citokinvihart vált ki. Mindezeket összefüggésbe hozták a vírus okozta súlyos megbetegedéssel és halállal.

- REF: Fierz, Walter Fierz és Walz, Brigitte Walz. "Az eredeti antigénbűn miatti antitestfüggő felerősödés és a SARS kialakulása" Front. Immunol. 2020. június 05. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01120/full.

- REF: Monto, Arnold S. et al. The Journal of Infectious Diseases. Vol. 215,12 (2017): 1782-1788. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5853211/#CIT0002.

- REF: Vatti A, et al: A comprehensive review." J Autoimmune. 2017 Sep;83:12-21. https://pubmed.ncbi.nlm.nih.gov/28479213/. https://pubmed.ncbi.nlm.nih.gov/28479213/

MOI #16

Az oltások széles körű alkalmazása nem semlegesítő antitesteket eredményez, és virulens mutáns vírus szerotípusokhoz (törzsekhez) vezethet.

- A magas vírusszaporodási sebesség kombinációja olyan egyéneknél, akik szuboptimális, nem semlegesítő antitesteket termelnek, pontosan azt a környezetet teremti meg, amelyben a rezisztens vírusok valószínűleg kialakulnak és terjednek.

  - REF: Moore, John. "Megközelítések a különböző COVID-19 vakcinák optimális felhasználásához: A vírusváltozatok és a vakcina hatékonyságának kérdései." JAMA. Online közzététel: 2021. március 4. https://jamanetwork.com/journals/jama/fullarticle/2777390.

- Az mRNS injekciókra adott antitestválasz magasabb, mint a lábadozó (gyógyuló) egyéneknél tapasztalt titerek. Ez a nem semlegesítő antitestek magas arányát eredményezi.

  - REF: Amana, Fatima et al . "A SARS-CoV-2 mRNS-vakcinációra adott plazmablasztikus választ a nem-neutralizáló antitestek dominálják, amelyek mind az NTD-t, mind az RBD-t célozzák." medRxiv 2021.03.07.21253098. https://www.medrxiv.org/content/10.1101/2021.03.07.21253098v1.full

Grant Final Report

Grant ID: R18 HS 017045

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS)

Inclusive dates: 12/01/07 - 09/30/10

Principal Investigator:
Lazarus, Ross, MBBS, MPH, MMed, GDCompSci

Team members:
Michael Klompas, MD, MPH

Performing Organization:
Harvard Pilgrim Health Care, Inc.

Project Officer:
Steve Bernstein

Submitted to:
The Agency for Healthcare Research and Quality (AHRQ)
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Abstract

Purpose: To develop and disseminate HIT evidence and evidence-based tools to improve healthcare decision making through the use of integrated data and knowledge management.

Scope: To create a generalizable system to facilitate detection and clinician reporting of vaccine adverse events, in order to improve the safety of national vaccination programs.

Methods: Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice were used. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions were evaluated for values suggestive of an adverse event.

Results: Restructuring at CDC and consequent delays in terms of decision making have made it challenging despite best efforts to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial and comparison of ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. However, Preliminary data were collected and analyzed and this initiative has been presented at a number of national symposia.

Key Words: electronic health records, vaccinations, adverse event reporting

Final Report

Purpose

This research project was funded to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS), via the following aims:

Aim 1. Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration.

Aim 2. Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS).

Aim 3. Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.

Aim 4. Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.

Scope

Public and professional confidence in vaccination depends on reliable postmarketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). This project is serving as an extension of the Electronic Support for Public Health (ESP) project, an automated system using electronic health record (EHR) data to detect and securely report cases of certain diseases to a local public health authority. ESP provides a ready-made platform for automatically converting clinical, laboratory, prescription, and demographic data from almost any EHR system into database tables on a completely independent server, physically located and secured by the same logical and physical security as the EHR data itself. The ESP:VAERS project developed criteria and algorithms to identify important adverse events related to vaccinations in ambulatory care EHR data, and made attempts at formatting and securely sending electronic VAERS reports directly to the Centers for Disease Control and Prevention (CDC).

Patient data were available from Epic System's Certification Commission for Health Information Technology-certified EpicCare system at all ambulatory care encounters within Atrius Health, a large multispecialty group practice with over 35 facilities. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions are evaluated for values

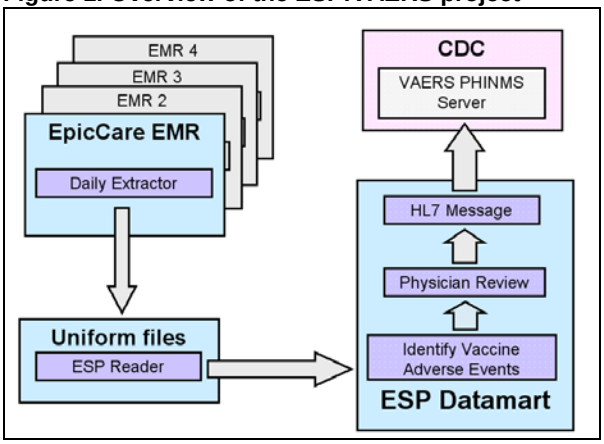
suggestive of an adverse vaccine event. When a possible adverse event was detected, it was recorded, and the appropriate clinician was to be notified electronically.

Clinicians in-basket messaging was designed to provide a preview a pre-populated report with information from the EHR about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment regarding whether they wish to send a report to VAERS. Clinicians would then have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. The CDC's Public Health Information Network Messaging System (PHIN-MS) software was installed within the facilities so that the approved reports could be securely transferred to VAERS as electronic messages in an interoperable health data exchange format using Health Level 7 (HL7).

Methods

The goal of Aim 1: *Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration,* and Aim 2: *Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS),* was to construct the below flow of data in order to support the first two Aims:

Figure 1. Overview of the ESP:VAERS project



Existing and functioning ESP components are shown on the left, and Aims 1 and 2 on the right. ESP:VAERS flags every vaccinated patient, and prospectively accumulate that patient's diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions. A main component of Aim 1 was to *Develop AE criteria to assess these parameters for new or abnormal values that might be suggestive of an adverse effect.* A reporting protocol & corresponding algorithms were developed to detect potential adverse event cases using diagnostic codes, and methods were tested to identify prescriptions or abnormal laboratory values that might be suggestive of an adverse effect. These algorithms were designed to seek both expected and unexpected adverse effects.

This reporting protocol was approved by both internal & external partners. We initially prepared a draft document describing the elements, algorithms, interval of interest after vaccination, and actions for broad classes of post-vaccination events, including those to be reported immediately without delay (such as acute anaphylactic reaction following vaccination), those never to be reported (such as routine check-ups following vaccination) and those to be reported at the discretion and with additional information from the attending physician through a feedback mechanism. The draft was then widely circulated as an initial / working draft for comment by relevant staff in the CDC and among our clinical colleagues at Atrius. In addition to review by the internal CDC Brighton Collaboration liaison, this protocol has also received review & comment via the CDC's Clinical Immunization Safety Assessment (CISA) Network.

The goal of Aim 2 was the *Development of HL7 messages code for ESP:VAERS to ensure secure transmission to CDC via PHIN-MS*. The HL7 specification describing the elements for an electronic message to be submitted to Constella, the consultants engaged by CDC for this project was implemented. Synthetic and real test data was been generated and transmitted between Harvard and Constella. However, real data transmissions of non-physician approved reports to the CDC was unable to commence, as by the end of this project, the CDC had yet to respond to multiple requests to partner for this activity.

The goal of Aim 3 was to *Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.*

We had initially planned to evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project—a collaborative effort between CDC's Immunization Safety Office and eight large managed care organizations. Through a randomized trial, we would also test the hypothesis that the combination of secure, computer-assisted, clinician-approved, adverse event detection, and automated electronic reporting will substantially increase the number, completeness, validity, and timeliness of physician-approved case reports to VAERS compared to the existing spontaneous reporting system; however, due to restructuring at CDC and consequent delays in terms of decision making, it became impossible to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial, and compare ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. Therefore, the components under this particular Aim were not achieved.

Aim 4 *Distribution of documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems* has been successfully completed. Functioning source code is available to share under an approved open source license. ESP:VAERS source code is available as part of the ESP source code distribution. It is licensed under the LGPL, an open source license compatible with commercial use. We have added the ESP:VAERS code, HL7 and other specifications and documentation to the existing ESP web documentation and distribution resource center http://esphealth.org, specifically, the Subversion repository available at:
http://esphealth.org/trac/ESP/wiki/ESPVAERS.

Results

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions (2.6 percent of vaccinations) were identified. This is an average of 890 possible events, an average of 1.3 events per clinician, per month. These data were presented at the 2009 AMIA conference.

In addition, ESP:VAERS investigators participated on a panel to explore the perspective of clinicians, electronic health record (EHR) vendors, the pharmaceutical industry, and the FDA towards systems that use proactive, automated adverse event reporting.

Adverse events from drugs and vaccines are common, but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of "problem" drugs and vaccines that endanger public health. New surveillance methods for drug and vaccine adverse effects are needed. Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report, as well as the burdens of reporting: reporting is not part of clinicians' usual workflow, takes time, and is duplicative. Proactive, spontaneous, automated adverse event reporting imbedded within EHRs and other information systems has the potential to speed the identification of problems with new drugs and more careful quantification of the risks of older drugs.

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

Inclusion of AHRQ Priority Populations

The focus of our project was the Atrius Health (formerly HealthOne) provider & patient community. This community serves several AHRQ inclusion populations, specifically low-income and minority populations in primarily urban settings.

Atruis currently employs approximately 700 physicians to serve 500,000 patients at more than 18 office sites spread throughout the greater Metropolitan Boston area. The majority of Atruis physicians are primary care internal medicine physicians or pediatricians but the network also includes physicians from every major specialty.

The entire adult and pediatric population served by Atruis was included in our adverse event surveillance system (ESP:VAERS). Atruis serves a full spectrum of patients that reflects the broad diversity of Eastern Massachusetts. A recent analysis suggests that the population served by Atruis is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the Atruis population is under age 18.

List of Publications and Products

ESP:VAERS [source code available as part of the ESP source code distribution]. Licensed under the GNU Lesser General Public License (LGPL), an open source license compatible with commercial use. Freely available under an approved open source license at: http://esphealth.org.

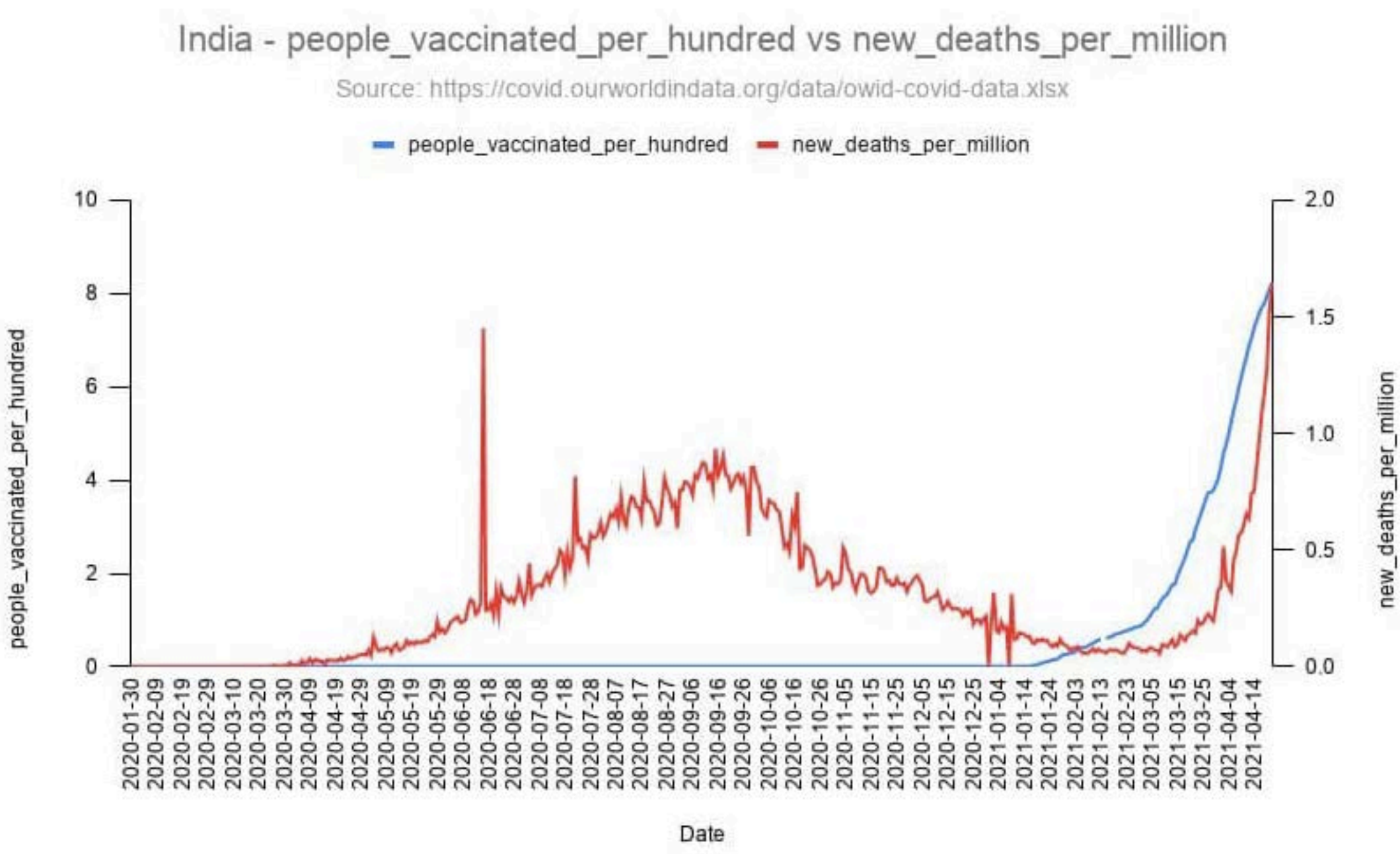
Lazarus, R, Klompas M, Hou X, Campion FX, Dunn J, Platt R. Automated Electronic Detection & Reporting of Adverse Events Following Vaccination: ESP:VAERS. The CDC Vaccine Safety Datalink (VSD) Annual Meeting. Atlanta, GA; April, 2008.

Lazarus R, Klompas M Automated vaccine adverse event detection and reporting from electronic medical records. CDC Public Health Informatics Network (PHIN) Conference August 27, 2008.

Klompas M, Lazarus R ESP:VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 November 17th.

Lazarus R, Klompas M, Kruskal B, Platt R Temporal patterns of fever following immunization in ambulatory care data identified by ESP:VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.

Linder J, Klompas M, Cass B, et al. Spontaneous Electronic Adverse Event Reporting: Perspectives from Clinicians, EHR Vendors, Biopharma, and the FDA. Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.


India - people_vaccinated_per_hundred vs new_deaths_per_million
Source: https://covid.ourworldindata.org/data/owid-covid-data.xlsx
people_vaccinated_per_hundred
new_deaths_per_million
people_vaccinated_per_hundred
new_deaths_per_million
Date

FACT SHEET FOR RECIPIENTS AND CAREGIVERS
EMERGENCY USE AUTHORIZATION (EUA) OF THE MODERNA COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19) IN INDIVIDUALS 18 YEARS OF AGE AND OLDER

You are being offered the Moderna COVID-19 Vaccine to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the Moderna COVID-19 Vaccine, which you may receive because there is currently a pandemic of COVID-19.

The Moderna COVID-19 Vaccine is a vaccine and may prevent you from getting COVID-19. There is no U.S. Food and Drug Administration (FDA) approved vaccine to prevent COVID-19.

Read this Fact Sheet for information about the Moderna COVID-19 Vaccine. Talk to the vaccination provider if you have questions. It is your choice to receive the Moderna COVID-19 Vaccine.

The Moderna COVID-19 Vaccine is administered as a 2-dose series, 1 month apart, into the muscle.

The Moderna COVID-19 Vaccine may not protect everyone.

This Fact Sheet may have been updated. For the most recent Fact Sheet, please visit www.modernatx.com/covid19vaccine-eua.

WHAT YOU NEED TO KNOW BEFORE YOU GET THIS VACCINE

WHAT IS COVID-19?
COVID-19 is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

WHAT IS THE MODERNA COVID-19 VACCINE?
The Moderna COVID-19 Vaccine is an unapproved vaccine that may prevent COVID-19. There is no FDA-approved vaccine to prevent COVID-19.

The FDA has authorized the emergency use of the Moderna COVID-19 Vaccine to prevent COVID-19 in individuals 18 years of age and older under an Emergency Use Authorization (EUA).

For more information on EUA, see the "**What is an Emergency Use Authorization (EUA)?**" section at the end of this Fact Sheet.

WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET THE MODERNA COVID-19 VACCINE?

Tell your vaccination provider about all of your medical conditions, including if you:

- have any allergies
- have a fever
- have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects your immune system
- are pregnant or plan to become pregnant
- are breastfeeding
- have received another COVID-19 vaccine

WHO SHOULD GET THE MODERNA COVID-19 VACCINE?

FDA has authorized the emergency use of the Moderna COVID-19 Vaccine in individuals 18 years of age and older.

WHO SHOULD NOT GET THE MODERNA COVID-19 VACCINE?

You should not get the Moderna COVID-19 Vaccine if you:

- had a severe allergic reaction after a previous dose of this vaccine
- had a severe allergic reaction to any ingredient of this vaccine

WHAT ARE THE INGREDIENTS IN THE MODERNA COVID-19 VACCINE?

The Moderna COVID-19 Vaccine contains the following ingredients: messenger ribonucleic acid (mRNA), lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose.

HOW IS THE MODERNA COVID-19 VACCINE GIVEN?

The Moderna COVID-19 Vaccine will be given to you as an injection into the muscle.

The Moderna COVID-19 Vaccine vaccination series is 2 doses given 1 month apart.

If you receive one dose of the Moderna COVID-19 Vaccine, you should receive a second dose of the same vaccine 1 month later to complete the vaccination series.

HAS THE MODERNA COVID-19 VACCINE BEEN USED BEFORE?

The Moderna COVID-19 Vaccine is an unapproved vaccine. In clinical trials, approximately 15,400 individuals 18 years of age and older have received at least 1 dose of the Moderna COVID-19 Vaccine.

WHAT ARE THE BENEFITS OF THE MODERNA COVID-19 VACCINE?

In an ongoing clinical trial, the Moderna COVID-19 Vaccine has been shown to prevent COVID-19 following 2 doses given 1 month apart. The duration of protection against COVID-19 is currently unknown.

WHAT ARE THE RISKS OF THE MODERNA COVID-19 VACCINE?
Side effects that have been reported with the Moderna COVID-19 Vaccine include:

- Injection site reactions: pain, tenderness and swelling of the lymph nodes in the same arm of the injection, swelling (hardness), and redness
- General side effects: fatigue, headache, muscle pain, joint pain, chills, nausea and vomiting, and fever

There is a remote chance that the Moderna COVID-19 Vaccine could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose of the Moderna COVID-19 Vaccine. For this reason, your vaccination provider may ask you to stay at the place where you received your vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of your face and throat
- A fast heartbeat
- A bad rash all over your body
- Dizziness and weakness

These may not be all the possible side effects of the Moderna COVID-19 Vaccine. Serious and unexpected side effects may occur. The Moderna COVID-19 Vaccine is still being studied in clinical trials.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?
If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

Call the vaccination provider or your healthcare provider if you have any side effects that bother you or do not go away.

Report vaccine side effects to **FDA/CDC Vaccine Adverse Event Reporting System (VAERS)**. The VAERS toll-free number is 1-800-822-7967 or report online to https://vaers.hhs.gov/reportevent.html. Please include "Moderna COVID-19 Vaccine EUA" in the first line of box #18 of the report form.

In addition, you can report side effects to ModernaTX, Inc. at 1-866-MODERNA (1-866-663-3762).

You may also be given an option to enroll in **v-safe. V-safe** is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. **V-safe** asks questions that help CDC monitor the safety of COVID-19 vaccines. **V-safe** also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information on how to sign up, visit: www.cdc.gov/vsafe.

WHAT IF I DECIDE NOT TO GET THE MODERNA COVID-19 VACCINE?
It is your choice to receive or not receive the Moderna COVID-19 Vaccine. Should you decide not to receive it, it will not change your standard medical care.

ARE OTHER CHOICES AVAILABLE FOR PREVENTING COVID-19 BESIDES MODERNA COVID-19 VACCINE?
Currently, there is no FDA-approved alternative vaccine available for prevention of COVID-19. Other vaccines to prevent COVID-19 may be available under Emergency Use Authorization.

CAN I RECEIVE THE MODERNA COVID-19 VACCINE WITH OTHER VACCINES?
There is no information on the use of the Moderna COVID-19 Vaccine with other vaccines.

WHAT IF I AM PREGNANT OR BREASTFEEDING?
If you are pregnant or breastfeeding, discuss your options with your healthcare provider.

WILL THE MODERNA COVID-19 VACCINE GIVE ME COVID-19?
No. The Moderna COVID-19 Vaccine does not contain SARS-CoV-2 and cannot give you COVID-19.

KEEP YOUR VACCINATION CARD
When you receive your first dose, you will get a vaccination card to show you when to return for your second dose of the Moderna COVID-19 Vaccine. Remember to bring your card when you return.

ADDITIONAL INFORMATION
If you have questions, visit the website or call the telephone number provided below.

To access the most recent Fact Sheets, please scan the QR code provided below.

Moderna COVID-19 Vaccine website	Telephone number
www.modernatx.com/covid19vaccine-eua	1-866-MODERNA (1-866-663-3762)

HOW CAN I LEARN MORE?
- Ask the vaccination provider
- Visit CDC at https://www.cdc.gov/coronavirus/2019-ncov/index.html
- Visit FDA at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- Contact your state or local public health department

WHERE WILL MY VACCINATION INFORMATION BE RECORDED?
The vaccination provider may include your vaccination information in your state/local jurisdiction's Immunization Information System (IIS) or other designated system. This will ensure that you receive the same vaccine when you return for the second dose. For more information about IISs, visit: https://www.cdc.gov/vaccines/programs/iis/about.html.

WHAT IS THE COUNTERMEASURES INJURY COMPENSATION PROGRAM?
The Countermeasures Injury Compensation Program (CICP) is a federal program that may help pay for costs of medical care and other specific expenses of certain people who have been seriously injured by certain medicines or vaccines, including this vaccine. Generally, a claim must be submitted to the CICP within one (1) year from the date of receiving the vaccine. To learn more about this program, visit www.hrsa.gov/cicp/ or call 1-855-266-2427.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?
The United States FDA has made the Moderna COVID-19 Vaccine available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Services (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

The Moderna COVID-19 Vaccine has not undergone the same type of review as an FDA-approved or cleared product. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of the scientific evidence available showing that the product may be effective to prevent COVID-19 during the COVID-19 pandemic and that the known and potential benefits of the product outweigh the known and potential risks of the product. All of these criteria must be met to allow for the product to be used during the COVID-19 pandemic.

The EUA for the Moderna COVID-19 Vaccine is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

Patent(s): www.modernatx.com/patents
Revised: 12/2020

Scan to capture that this Fact Sheet was provided to vaccine recipient for the electronic medical records/immunization information systems.
Barcode Date: 12/2020

FACT SHEET FOR RECIPIENTS AND CAREGIVERS

EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19) IN INDIVIDUALS 16 YEARS OF AGE AND OLDER

You are being offered the Pfizer-BioNTech COVID-19 Vaccine to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the Pfizer-BioNTech COVID-19 Vaccine, which you may receive because there is currently a pandemic of COVID-19.

The Pfizer-BioNTech COVID-19 Vaccine is a vaccine and may prevent you from getting COVID-19. There is no U.S. Food and Drug Administration (FDA) approved vaccine to prevent COVID-19.

Read this Fact Sheet for information about the Pfizer-BioNTech COVID-19 Vaccine. Talk to the vaccination provider if you have questions. It is your choice to receive the Pfizer-BioNTech COVID-19 Vaccine.

The Pfizer-BioNTech COVID-19 Vaccine is administered as a 2-dose series, 3 weeks apart, into the muscle.

The Pfizer-BioNTech COVID-19 Vaccine may not protect everyone.

This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.cvdvaccine.com.

WHAT YOU NEED TO KNOW BEFORE YOU GET THIS VACCINE

WHAT IS COVID-19?

COVID-19 disease is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

WHAT IS THE PFIZER-BIONTECH COVID-19 VACCINE?

The Pfizer-BioNTech COVID-19 Vaccine is an unapproved vaccine that may prevent COVID-19. There is no FDA-approved vaccine to prevent COVID-19.

The FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19 in individuals 16 years of age and older under an Emergency Use Authorization (EUA).

For more information on EUA, see the "**What is an Emergency Use Authorization (EUA)?**" section at the end of this Fact Sheet.

WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET THE PFIZER-BIONTECH COVID-19 VACCINE?

Tell the vaccination provider about all of your medical conditions, including if you:

- have any allergies
- have a fever
- have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects your immune system
- are pregnant or plan to become pregnant
- are breastfeeding
- have received another COVID-19 vaccine

WHO SHOULD GET THE PFIZER-BIONTECH COVID-19 VACCINE?

FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine in individuals 16 years of age and older.

WHO SHOULD <u>NOT</u> GET THE PFIZER-BIONTECH COVID-19 VACCINE?

You should not get the Pfizer-BioNTech COVID-19 Vaccine if you:

- had a severe allergic reaction after a previous dose of this vaccine
- had a severe allergic reaction to any ingredient of this vaccine.

WHAT ARE THE INGREDIENTS IN THE PFIZER-BIONTECH COVID-19 VACCINE?

The Pfizer-BioNTech COVID-19 Vaccine includes the following ingredients: mRNA, lipids ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose.

HOW IS THE PFIZER-BIONTECH COVID-19 VACCINE GIVEN?

The Pfizer-BioNTech COVID-19 Vaccine will be given to you as an injection into the muscle.

The Pfizer-BioNTech COVID-19 Vaccine vaccination series is 2 doses given 3 weeks apart.

If you receive one dose of the Pfizer-BioNTech COVID-19 Vaccine, you should receive a second dose of this same vaccine 3 weeks later to complete the vaccination series.

HAS THE PFIZER-BIONTECH COVID-19 VACCINE BEEN USED BEFORE?
The Pfizer-BioNTech COVID-19 Vaccine is an unapproved vaccine. In clinical trials, approximately 20,000 individuals 16 years of age and older have received at least 1 dose of the Pfizer-BioNTech COVID-19 Vaccine.

WHAT ARE THE BENEFITS OF THE PFIZER-BIONTECH COVID-19 VACCINE?
In an ongoing clinical trial, the Pfizer-BioNTech COVID-19 Vaccine has been shown to prevent COVID-19 following 2 doses given 3 weeks apart. The duration of protection against COVID-19 is currently unknown.

WHAT ARE THE RISKS OF THE PFIZER-BIONTECH COVID-19 VACCINE?
Side effects that have been reported with the Pfizer-BioNTech COVID-19 Vaccine include:

- injection site pain
- tiredness
- headache
- muscle pain
- chills
- joint pain
- fever
- injection site swelling
- injection site redness
- nausea
- feeling unwell
- swollen lymph nodes (lymphadenopathy)

There is a remote chance that the Pfizer-BioNTech COVID-19 Vaccine could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose of the Pfizer-BioNTech COVID-19 Vaccine. For this reason, your vaccination provider may ask you to stay at the place where you received your vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of your face and throat
- A fast heartbeat
- A bad rash all over your body
- Dizziness and weakness

These may not be all the possible side effects of the Pfizer-BioNTech COVID-19 Vaccine. Serious and unexpected side effects may occur. Pfizer-BioNTech COVID-19 Vaccine is still being studied in clinical trials.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?
If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

Call the vaccination provider or your healthcare provider if you have any side effects that bother you or do not go away.

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. Please include "Pfizer-BioNTech COVID-19 Vaccine EUA" in the first line of box #18 of the report form.

In addition, you can report side effects to Pfizer Inc. at the contact information provided below.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

You may also be given an option to enroll in v-safe. V-safe is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information on how to sign up, visit: www.cdc.gov/vsafe.

WHAT IF I DECIDE NOT TO GET THE PFIZER-BIONTECH COVID-19 VACCINE?
It is your choice to receive or not receive the Pfizer-BioNTech COVID-19 Vaccine. Should you decide not to receive it, it will not change your standard medical care.

ARE OTHER CHOICES AVAILABLE FOR PREVENTING COVID-19 BESIDES PFIZER-BIONTECH COVID-19 VACCINE?
Currently, there is no approved alternative vaccine available for prevention of COVID-19. Other vaccines to prevent COVID-19 may be available under Emergency Use Authorization.

CAN I RECEIVE THE PFIZER-BIONTECH COVID-19 VACCINE WITH OTHER VACCINES?
There is no information on the use of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

WHAT IF I AM PREGNANT OR BREASTFEEDING?
If you are pregnant or breastfeeding, discuss your options with your healthcare provider.

WILL THE PFIZER-BIONTECH COVID-19 VACCINE GIVE ME COVID-19?
No. The Pfizer-BioNTech COVID-19 Vaccine does not contain SARS-CoV-2 and cannot give you COVID-19.

KEEP YOUR VACCINATION CARD
When you get your first dose, you will get a vaccination card to show you when to return for your second dose of Pfizer-BioNTech COVID-19 Vaccine. Remember to bring your card when you return.

ADDITIONAL INFORMATION
If you have questions, visit the website or call the telephone number provided below.

To access the most recent Fact Sheets, please scan the QR code provided below.

Global website	Telephone number
www.cvdvaccine.com 	1-877-829-2619 (1-877-VAX-CO19)

HOW CAN I LEARN MORE?
- Ask the vaccination provider.
- Visit CDC at https://www.cdc.gov/coronavirus/2019-ncov/index.html.
- Visit FDA at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.
- Contact your local or state public health department.

WHERE WILL MY VACCINATION INFORMATION BE RECORDED?
The vaccination provider may include your vaccination information in your state/local jurisdiction's Immunization Information System (IIS) or other designated system. This will ensure that you receive the same vaccine when you return for the second dose. For more information about IISs visit: https://www.cdc.gov/vaccines/programs/iis/about.html.

WHAT IS THE COUNTERMEASURES INJURY COMPENSATION PROGRAM?
The Countermeasures Injury Compensation Program (CICP) is a federal program that may help pay for costs of medical care and other specific expenses of certain people who have been seriously injured by certain medicines or vaccines, including this vaccine. Generally, a claim must be submitted to the CICP within one (1) year from the date of receiving the vaccine. To learn more about this program, visit www.hrsa.gov/cicp/ or call 1-855-266-2427.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?
The United States FDA has made the Pfizer-BioNTech COVID-19 Vaccine available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Services (HHS) declaration that circumstances exist to

justify the emergency use of drugs and biological products during the COVID-19 pandemic.

The Pfizer-BioNTech COVID-19 Vaccine has not undergone the same type of review as an FDA-approved or cleared product. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that the product may be effective to prevent COVID-19 during the COVID-19 pandemic and that the known and potential benefits of the product outweigh the known and potential risks of the product. All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic.

The EUA for the Pfizer-BioNTech COVID-19 Vaccine is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

Manufactured by
Pfizer Inc., New York, NY 10017

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

LAB-1451-1.1

Revised: December 2020

Scan to capture that this Fact Sheet was provided to vaccine recipient for the electronic medical records/immunization information systems.

Barcode Date: 12/2020

Research Article ISSN 2639-9458

Microbiology & Infectious Diseases

COVID-19 RNA Based Vaccines and the Risk of Prion Disease

J. Bart Classen, MD*

Classen Immunotherapies, Inc., 3637 Rockdale Road, Manchester, MD 21102, E-mail: classen@vaccines.net.

***Correspondence:**
J. Bart Classen, MD, Classen Immunotherapies, Inc., 3637 Rockdale Road, Manchester, MD 21102, Tel: 410-377-8526.

Received: 27 December 2020; **Accepted:** 18 January 2021

Citation: Classen JB. COVID-19 RNA Based Vaccines and the Risk of Prion Disease. Microbiol Infect Dis. 2021; 5(1): 1-3.

ABSTRACT

Development of new vaccine technology has been plagued with problems in the past. The current RNA based SARS-CoV-2 vaccines were approved in the US using an emergency order without extensive long term safety testing. In this paper the Pfizer COVID-19 vaccine was evaluated for the potential to induce prion-based disease in vaccine recipients. The RNA sequence of the vaccine as well as the spike protein target interaction were analyzed for the potential to convert intracellular RNA binding proteins TAR DNA binding protein (TDP-43) and Fused in Sarcoma (FUS) into their pathologic prion conformations. The results indicate that the vaccine RNA has specific sequences that may induce TDP-43 and FUS to fold into their pathologic prion confirmations. In the current analysis a total of sixteen UG tandem repeats (ΨGΨG) were identified and additional UG (ΨG) rich sequences were identified. Two GGΨA sequences were found. Potential G Quadruplex sequences are possibly present but a more sophisticated computer program is needed to verify these. Furthermore, the spike protein, created by the translation of the vaccine RNA, binds angiotensin converting enzyme 2 (ACE2), a zinc containing enzyme. This interaction has the potential to increase intracellular zinc. Zinc ions have been shown to cause the transformation of TDP-43 to its pathologic prion configuration. The folding of TDP-43 and FUS into their pathologic prion confirmations is known to cause ALS, front temporal lobar degeneration, Alzheimer's disease and other neurological degenerative diseases. The enclosed finding as well as additional potential risks leads the author to believe that regulatory approval of the RNA based vaccines for SARS-CoV-2 was premature and that the vaccine may cause much more harm than benefit.

Keywords
COVID-19, Vaccines, Diabetes, Immunity.

Introduction
Vaccines have been found to cause a host of chronic, late developing adverse events. Some adverse events like type 1 diabetes may not occur until 3-4 years after a vaccine is administered [1]. In the example of type 1 diabetes the frequency of cases of adverse events may surpass the frequency of cases of severe infectious disease the vaccine was designed to prevent. Given that type 1 diabetes is only one of many immune mediated diseases potentially caused by vaccines, chronic late occurring adverse events are a serious public health issue.

The advent of new vaccine technology creates new potential mechanisms of vaccine adverse events. For example, the first killed polio vaccine actually caused polio in recipients because the up scaled manufacturing process did not effectively kill the polio virus before it was injected into patients. RNA based vaccines offers special risks of inducing specific adverse events. One such potential adverse event is prion based diseases caused by activation of intrinsic proteins to form prions. A wealth of knowledge has been published on a class of RNA binding proteins shown to participating in causing a number of neurological diseases including Alzheimer's disease and ALS. TDP-43 and FUS are among the best studied of these proteins [2].

The Pfizer RNA based COVID-19 vaccine was approved by the US FDA under an emergency use authorization without long term safety data. Because of concerns about the safety of this vaccine a study was performed to determine if the vaccine could potentially induce prion based disease.

Methods
Pfizer's RNA based vaccine against COVID-19 was evaluated for the potential to convert TDP-43 and or FUS to their prion based

disease causing states. The vaccine RNA was analyzed for the presence of sequences that can activate TDP-43 and FUS. The interaction of the transcribed spike protein with its target was analyzed to determine if this action could also activate TDP-43 and FUS.

Results

Analysis of the Pfizer vaccine against COVID-19 identified two potential risk factors for inducing prion disease is humans. The RNA sequence in the vaccine [3] contains sequences believed to induce TDP-43 and FUS to aggregate in their prion based conformation leading to the development of common neurodegerative diseases. In particular it has been shown that RNA sequences GGUA [4], UG rich sequences [5], UG tandem repeats [6], and G Quadruplex sequences [7], have increased affinity to bind TDP-43 and or FUS and may cause TDP-43 or FUS to take their pathologic configurations in the cytoplasm. In the current analysis a total of sixteen UG tandem repeats (ΨGΨG) were identified and additional UG (ΨG) rich sequences were identified. Two GGΨA sequences were found. G Quadruplex sequences are possibly present but sophisticated computer programs are needed to verify these.

The spike protein encoded by the vaccine binds angiotensin converting enzyme 2 (ACE2), an enzyme which contains zinc molecules [8]. The binding of spike protein to ACE2 has the potential to release the zinc molecule, an ion that causes TDP-43 to assume its pathologic prion transformation [9].

Discussion

There is an old saying in medicine that "the cure may be worse than the disease." The phrase can be applied to vaccines. In the current paper the concern is raised that the RNA based COVID vaccines have the potential to cause more disease than the epidemic of COVID-19. This paper focuses on a novel potential adverse event mechanism causing prion disease which could be even more common and debilitating than the viral infection the vaccine is designed to prevent. While this paper focuses on one potential adverse event there are multiple other potential fatal adverse events as discussed below.

Over the last two decades there has been a concern among certain scientists that prions could be used as bioweapons. More recently there has been a concern that ubiquitous intracellular molecules could be activated to cause prion disease including Alzheimer's disease, ALS and other neurodegenerative diseases. This concern originates due to potential for misuse of research data on the mechanisms by which certain RNA binding proteins like TDP-43, FUS and others can be activated to form disease causing prions. The fact that this research, which could be used for bioweapons development, is funded by private organizations including the Bill and Melinda Gates Foundation, and Ellison Medical Foundation [2] without national/international oversight is also a concern. In the past, for example, there were prohibitions for publishing information pertaining to construction of nuclear bombs.

Published data has shown that there are several different factors that can contribute to the conversion of certain RNA binding proteins including TDP-43, FUS and related molecules to their pathologic states. These RNA binding proteins have many functions and are found in both the nucleus and the cytoplasm. These binding proteins have amino acid regions, binding motifs that bind specific RNA sequences. Binding to certain RNA sequences when the proteins are in the cytoplasm is believed to causes the molecules to fold in certain ways leading to pathologic aggregation and prion formation in the cytoplasm [2]. The current analysis indicates Pfizer's RNA based COVID-19 vaccine contains many of these RNA sequences that have been shown to have high affinity for TDP-43 or FUS and have the potential to induce chronic degenerative neurological diseases.

Zinc binding to the RNA recognition motif of TDP-43 is another mechanism leading to formation of amyloid like aggregations [9]. The viral spike protein, coded by the vaccine RNA sequence, binds ACE2 an enzyme containing zinc molecules [8]. This interaction has the potential to increase intracellular zinc levels leading to prion disease. The initial binding could be between spike proteins on the surface of the cell transfected by the vaccine and ACE2 on the surface of an adjacent cell. The resulting complex may become internalized. Alternatively, the interaction could initially take place in the cytoplasm of a cell that makes ACE2 and has been transfected with the vaccine RNA coding for the spike protein. The interaction is quite concerning given the belief that the virus causing COVID-19, SARS-CoV-2, is a bioweapon [10,11] and it is possible that the viral spike protein may have been designed to cause prion disease.

Another related concern is that the Pfizer vaccine uses a unique RNA nucleoside 1-methyl-3'-pseudouridylyl (Ψ). According to FDA briefing documents, this nucleoside was chosen to reduce activation of the innate immune system [12]. RNA molecules containing this nucleoside will undoubtedly have altered binding [13]. Unfortunately, the effect on TDP-43, FUS and other RNA binding proteins is not published. The use of this nucleoside in a vaccine can potentially enhance the binding affinity of RNA sequences capable of causing TDP-43 and FUS to assume toxic configurations.

There are many other potential adverse events that can be induced by the novel RNA based vaccines against COVID-19. The vaccine places a novel molecule, spike protein, in/on the surface of host cells. This spike protein is a potential receptor for another possibly novel infectious agent. If those who argue that the COVID-19 is actually a bioweapon are correct, then a second potentially more dangerous virus may be released that binds spike protein found on the host cells of vaccine recipients. Data is not publicly available to provide information on how long the vaccine RNA is translated in the vaccine recipient and how long after translation the spike protein will be present in the recipient's cells. Such studies pertaining to in vivo expression will be complex and challenging. Genetic diversity protects species from mass casualties caused by infectious agents. One individual may be killed by a virus while

another may have no ill effects from the same virus. By placing the identical receptor, the spike protein, on cells of everyone in a population, the genetic diversity for at least one potential receptor disappears. Everyone in the population now becomes potentially susceptible to binding with the same infectious agent.

Autoimmunity and the opposing condition, metabolic syndrome, are well know adverse events caused by vaccines [14]. COVID-19 infections are associated with the induction of autoantibodies and autoimmune disease [15,16] making it more than plausible a vaccine could do the same. One author has found amino acid sequences coded by the spike protein to be identical to sequences in human proteins including proteins found in the CNS [17]. Autoimmunity can also be induced by epitope spreading when a foreign antigen, like the spike protein, is presented by an antigen presenting cell that also has self molecules attached to its MHC molecules.

Finally, others working in the field have published additional support that COVID-19 vaccines could potentially induce prion disease. Authors [18] found prion related sequences in the COVID-19 spike protein which were not found in related coronaviruses. Others [19] have reported a case of prion disease, Creutzfeldt-Jakob disease, initially occurring in a man with COVID-19.

Many have raised the warning that the current epidemic of COVID-19 is actually the result of an bioweapons attack released in part by individuals in the United States government [10,11]. Such a theory is not far fetched given that the 2001 anthrax attack in the US originated at Fort Detrick, a US army bioweapon facility. Because the FBI's anthrax investigation was closed against the advice of the lead FBI agent in the case, there are likely conspirators still working in the US government. In such a scenario the primary focus of stopping a bioweapons attack must be to apprehend the conspirators or the attacks will never cease. Approving a vaccine, utilizing novel RNA technology without extensive testing is extremely dangerous. The vaccine could be a bioweapon and even more dangerous than the original infection.

References

1. Classen JB, Classen DC. Clustering of cases of insulin dependent diabetes (IDDM) occurring three years after Hemophilus influenza B (HiB) immunization support causal relationship between immunization and IDDM. Autoimmunity. 2002; 35: 247-253.
2. King OD, Gitler AD, Shorter J. The tip of the iceberg: RNA-binding proteins with prion-like domains in neurodegenerative disease. Brain Res. 2012; 1462: 61-80.
3. WHO, International Non Proprietary Names Program: 11889. 9/2020.
4. Kapeli K, Pratt GA, Vu AQ, et al. Distinct and shared functions of ALS-associated proteins TDP-43, FUS and TAF15 revealed by multisystem analyses. Nature Communications. 2016; 7: 12143.
5. Kuo P, Chiang C, Wang Y, et al. The crystal structure of TDP-43 RRM1-DNA complex reveals the specific recognition for UG- and TG-rich nucleic acids. Nucleic Acids Research. 2014; 42: 4712-4722.
6. Tollervey JR, Curk T, Rogelj B, et al. Characterizing the RNA targets and position-dependent splicing regulation by TDP-43; implications for neurodegenerative diseases. Nat Neurosci. 2011; 14: 452-458.
7. Imperatore JA, McAninch DS, Valdez-Sinon AN, et al. FUS recognizes G quadruplex structures within neuronal mRNAs. Frontiers in Molecular Biosciences. 2020; 7: 6.
8. Shang J, Ye G, Shi K, et al. Structural basis of receptor recognition by SARS-CoV-2. Nature. 2020; 581: 221-225.
9. Garnier C, Devred F, Byrne D, et al. Zinc binding to RNA recognition motif of TDP-43 induces the formation of amyloid-like aggregates. Sci Rep. 2017; 7: 6812.
10. Classen JB. COVID-19, MMR vaccine, and bioweapons. Diabetes & its Complications.2020; 4: 1-8.
11. Classen JB. Evidence supporting the hypothesis that the 2019 epidemic of E-vaping acute lung injury (EVALI) was caused in part by COVID-19. Diabetes & Complications. 2020; 4: 1-2.
12. Pfizer-Biotech: COVID-19 Vaccine (BNT162, PF-07302048), Vaccines and Related Biological Products Advisory Committee Briefing Document. Meeting Date: 10 December 2020.
13. Roundtree IA, Evans ME, Pan, et al. Dynamic RNA modifications in gene expression regulation. Cell. 2017; 169: 1187-1200.
14. Classen JB. Review of Vaccine Induced Immune Overload and the Resulting Epidemics of Type 1 Diabetes and Metabolic Syndrome, Emphasis on Explaining the Recent accelerations in the Risk of Prediabetes and other Immune Mediated Diseases. J Mol Genet Med. 2014; S1: 025.
15. Amiral J. Can COVID-19 Induce an autoimmune disease associated with long- lasting symptoms and delayed complications? Ann Clin Immunol Microbiol. 2020; 2: 1014.
16. Wang EY, Mao T, Klein J, et al. Diverse functional autoantibodies in patients with COVID-19. medRxiv preprint. 2020.
17. Lyons-Weiler J. Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity. Journal of Translational Autoimmunity. 2020; 3: 100051.
18. Tetz G, Tetz V. SARS-CoV-2 prion-like domains in spike proteins enable higher affinity to ACE2. Preprint. 2020.
19. Young MJ, O'Hare M, Matiello M, et al. Creutzfeldt-Jakob disease in a man with COVID-19: SARS-CoV-2-accelerated neuro degeneration? Brain, Behavior, and Immunity. 2020; 89: 601-603.

20 Mechanisms of Injuries (MOI)
How COVID-19 Injections Can Make You Sick; Even Kill You

By Dr. Sherri Tenpenny
Cleveland, Ohio
www.DrTenpenny.com

Definitions:

J&J – Johnson and Johnson – uses adenovirus and transgene to create the spike protein
AZ – AstraZeneca – uses adenovirus and transgene to create spike proteins; high risk of blood clots
Pfizer and Moderna – use mRNA to create the spike protein
Spike protein – antigen on surface of the SARS-CoV2 virus that binds to the ACE2 receptors on the surface of cells to enter into organs to start replication.
Anti-S-Antibody – the antibody generated by your immune system B-cells after being exposed to the Spike protein; the antibody is supposed to bind to the spike protein on the surface of the virus to block entrance into the cells. However it is not known if this actually occurs.

MOI #1 – Injections can lead to death through anaphylactic shock, a life-threatening allergic reaction. With COVID shots, the allergic reaction is suspected to be caused by previous exposure to and sensitization to polyethylene glycol [PEG].

MOI #2 – Anti-Inflammatory macrophages, called M2, are inhibited by anti-spike-antibodies [anti-S-Ab].

MOI #3 – All COVID shots lead to the creation of a spike protein through a process called translation. The spike protein can damage the body by **at least FOUR pathways:**

1. The spike protein behaves as a hapten, a small molecule that binds to the surface of organs, leading to an autoimmune response.
2. The spike protein can damage organs directly by promoting cardiovascular complications, damaging blood vessels in the lungs, and breaking through the blood brain barrier (BBB), important for protecting the brain.
3. The spike protein can incorporate into human DNA through a process called transfection.
4. The spike protein evokes the release of destructive anti-spike-antibodies, [anti-S-Ab] discussed below.

MOI #4 – Spike protein can trigger changes in blood vessel walls, leading to **pulmonary artery hypertension (PAH**), which is fatal even under the best current conventional and alternative treatments.

MOI #5 – In men, the **spike protein** can bind to the ACE2 receptor on sperm. **Risk of infertility** is indicated but not yet proven.

MOI #6 – Spike proteins cause inflammation and disruption of the **blood brain barrier (BBB),** leading to **neuropathology and brain degeneration.**

MOI #7 – Neurological degeneration: spike proteins can damage the *FUS* gene and mutate the *TDP-43 protein*, leading to **Amyotrophic Lateral Sclerosis (ALS).**

MOI #8 – Neurological degeneration: mutation and altered function of the TDP-43 protein can also lead to frontotemporal lobe degeneration (FTLD), **a cluster of chronic, degenerative neurological diseases.**

MOI #9 – Mutation of the *FUS* gene can also lead to **cancer.**

MOI #10 – **Adenoviruses** used in both the Johnson & Johnson shot and the AstraZeneca shots pose **a risk of cancer**.

MOI #11 – Anti-spike-antibodies **[anti-S-Ab]** can cause significant damage, specifically to the lungs. The antibodies can also cross-react with **28 different human tissue types**, establishing a mechanism for **multi-system autoimmune disorders and multiorgan failure.**

MOI #12 – Previous coronavirus exposure and the concept called **'original antigenic sin'** stops true protection against the SARS-CoV2 if previously ill with a coronavirus infection.

MOI #13 – There is an **increased risk of COVID illness and COVID-related death** in persons who has been previously vaccinated with an **influenza vaccine.**

MOI #14 – The larger (highly elevated) SARS-CoV-2 antibody response from a COVID infection or from a COVID shot, **results in prolonged and more severe illness.**

MOI #15 – COVID shots can lead to **enlarged lymph nodes** that may have long term ramifications.

MOI #16 – Widespread use of COVID shots results **in non-neutralizing antibodies**, especially in people who have already had a COVID infection. This may be leading to **virulent mutant viruses.**

MOI #17 – **Antibody Dependent Enhancement (ADE)** is a phenomenon occurs when a person is exposed to a circulating coronavirus after being vaccinated. The anti-S-Ab enhances the entry of the SARS-CoV-2 virus into the cell (usually macrophages) and accelerates its replication, causing more severe illness than they would have experienced if they had not been vaccinated.

MOI #18 – Johnson/Johnson and AstraZeneca shots release **a transgene** that can lead to potentially deadly side effects from injecting raw genetic material that **can induce anti-DNA antibodies and can integrate into human DNA.**

MOI #19 – Both Johnson/Johnson and AstraZeneca shots carry a snip of double stranded DNA (dsDNA) [transgene] wrapped in an adenovirus outer "shell." 50-billion particles are injected with each injection. dsDNA-antibodies are diagnostic of a long list of autoimmune disorders.

MOI #20: The AstraZeneca shot has been known to be associated with potentially deadly blood clots, a condition named Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT).

++++++++++++++++++

"Approving a vaccine, utilizing novel RNA technology without extensive testing is extremely dangerous. The vaccine could be a bioweapon and even more dangerous than the original infection."

REF: Classen JB. COVID-19 RNA Based Vaccines and the Risk of Prion Disease. Microbiol Infect Dis. 2021; 5(1): 1-3. https://scivisionpub.com/pdfs/covid19-rna-based-vaccines-and-the-risk-of-prion-disease-1503.pdf

By Dr. Sherri Tenpenny
Cleveland, Ohio

20 Mechanisms of Injuries (MOI)

How COVID-19 Injections Can Make You Sick...Even Kill You

$14.95

www.DrTenpenny.com

DISCLAIMER:

The information contained herein is intended for educational purposes and for course participants only. No portion of this ebook may be reproduced, stored in a retrieval system, or transmitted in any form by any means electronic, mechanical, photocopying, recording, or any other style without the prior written permission from Dr Sherri Tenpenny.

The information presented reflects the author's opinions at the time this ebook and course were created. Some information will change over time, as new research, data and science become available.

The author assumes no responsibility for updating the information contained herein. Future information may modify any information presented herein. All information regarding COVID 19, COVID 19 treatments, and/or COVID 19 injections is based solely on the author's opinion as a physician. The author's opinion reflects information that is currently available and in the public domain at the time of this production.

May 6, 2021

MOI #1: Injections can lead to death through anaphylactic shock, a life-threatening allergic reaction. With COVID shots, the allergic reaction is suspected to be caused by previous exposure to and sensitization to polyethylene glycol [PEG].

MOI #2: Anti-Inflammatory macrophages, called M2, are inhibited by anti-spike-antibodies **[anti-S-Ab]**

MOI #3: All COVID shots lead to the creation of a **spike protein** through a process called **translation**. The spike protein can damage the body by at least **FOUR** pathways:

1. The spike protein behaves as a **hapten**, a small molecule that binds to the surface of organs, leading to an autoimmune response.
2. The spike protein can **damage organs** directly by promoting cardiovascular complications, damaging blood vessels in the lungs, and breaking through the **blood brain barrier (BBB),** important for protecting the brain.
3. The spike protein can **incorporate into human DNA** through a process called **transfection.**
4. The spike protein evokes the release of **destructive anti-spike-antibodies, [anti-S-Ab]** discussed below.

MOI #4: Spike protein can trigger changes in blood vessel walls, leading to **pulmonary artery hypertension (PAH)**, which is fatal even under the best current conventional and alternative treatments.

MOI #5: The spike protein can bind to the ACE2 receptor on surface of **sperm and ovaries**. Risk of infertility is high but not yet proven.

MOI #6: Spike proteins cause inflammation and disruption of the **blood brain barrier (BBB),** leading to **neuropathology and brain degeneration.**

MOI #7: Neurological degeneration: spike proteins can damage the *FUS* gene and mutate the *TDP-43 protein,* leading to **Amyotrophic Lateral Sclerosis (ALS).**

MOI #8: Neurological degeneration: mutation and altered function of the *TDP-43 protein* can also lead to **frontotemporal lobe degeneration (FTLD)**, **a cluster of chronic, degenerative neurological diseases.**

MOI #9: Mutation of the *FUS* gene can also lead to **cancer.**

MOI #10: **Adenoviruses** used in both the Johnson & Johnson shot and the AstraZeneca shots pose a **risk of cancer.**

MOI #11: Anti-spike-antibodies [**anti-S-Ab**] can cause significant organ damage, specifically to the lungs. The antibodies can also cross-react with **28 different human tissue types,** establishing a mechanism for **multi-system autoimmune disorders and multi-organ failure.**

MOI #12: Previous coronavirus exposure and the concept called '**original antigenic sin'** stops true protection against the SARS-CoV-2 if a person has been previously ill with a common coronavirus infection.

MOI #13: There is an increased risk of COVID illness and COVID-related death in people who have had a previous **influenza vaccine.**

MOI #14: The larger (highly elevated) SARS-CoV-2 antibody response from a COVID infection or from a COVID shot, results in **prolonged and more severe illness.**

MOI #15: COVID shots can lead to **enlarged lymph nodes** that may have long term ramifications.

MOI #16: Widespread use of COVID shots results in **non-neutralizing antibodies,** especially in people who have already had a COVID infection. This may be leading to **virulent mutant viruses.**

MOI #17: Antibody Dependent Enhancement (ADE) is a phenomenon occurs when a person is exposed to a circulating coronavirus after being vaccinated. The **anti-S-Ab** enhances the entry of the SARS-CoV-2 virus into the cell (usually macrophages) and accelerates its replication, causing more severe illness than they would have experienced if they had not been vaccinated.

MOI #18: Johnson/Johnson and AstraZeneca shots release **a transgene** that can lead to potentially deadly side effects from injecting raw genetic material that **can induce anti-DNA antibodies and can integrate into human DNA.**

MOI #19: Both Johnson/Johnson and AstraZeneca shots carry a snip of double stranded DNA **(dsDNA) [transgene]** wrapped in an adenovirus outer "shell." **50-billion particles** are injected with each injection. **dsDNA-antibodies are diagnostic of a long list of autoimmune disorders.**

MOI #20 – The AstraZeneca shot has been known to be associated with potentially **deadly blood clots,** a condition named **Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT).**

"Approving a vaccine, utilizing novel RNA technology without extensive testing is extremely dangerous. The vaccine could be a bioweapon and even more dangerous than the original infection."

- **REF:** Classen JB. COVID-19 RNA Based Vaccines and the Risk of Prion Disease. Microbiol Infect Dis. 2021; 5(1):1-3. https://scivisionpub.com/pdfs/covid19-rna-based-vaccines-and-the-risk-of-prion-disease-1503.pdf

By injecting the synthetically made SARS-CoV-2 spike protein into the entire population through these genetic-modification injections, the risk of long-term side effects and risk of developing an autoimmune illness will remain for an unknown period of time. However, with B-cell priming and irreversible genetic manipulation, the risk for developing chronic illness or sudden death could last forever.

MOI #1 Anaphylactic shock

- Anaphylaxis is a severe, potentially life-threatening allergic reaction. It can occur within seconds or minutes of exposure to something you're allergic to, such as peanuts or bee stings.
- Injections can lead to death through anaphylactic shock, life-threatening allergic reactions. With COVID shots, the allergic reaction is suspected to be caused by previous sensitization to polyethylene glycol [PEG].
- **Polyethylene glycol (PEG)** is a water-soluble synthetic polymer consisting of repeating units of ethylene glycol. It is used to cover injected proteins to protect them from being broken down by enzymes.
- PEG is widely used in cosmetics, hygiene products, dental products, food and pharmaceuticals. There are 20 approved childhood and adults vaccines that contain polysorbate 20 or polysorbate 80.
- **PEG and polysorbate** are structurally related, and cross-reactive hypersensitivity between these compounds may occur.
- So many products now contain PEG, exposure is nearly unavoidable. Upward of 70% of the general public have anti-PEG antibodies compared with 0.2% two decades ago.
- Patients with high levels of anti-PEG IgG antibodies can experience severe allergic reactions and anaphylaxis when re-exposed to injected PEG.
- Known allergy to PEG, or polysorbate, is a contraindication to vaccination.

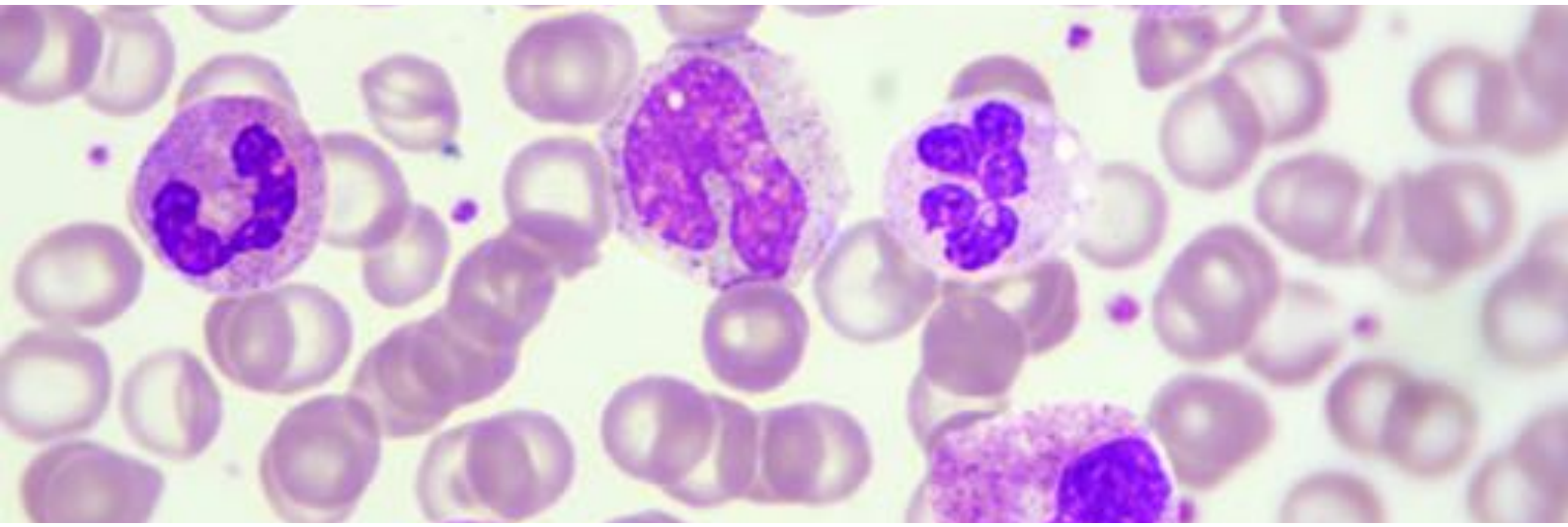
- REF: Moreno, Angelo, et al. “Anti-PEG Antibodies Inhibit the Anticoagulant Activity of PEGylated Aptamers.” Cell Chemical Biology. Vol 26, Issue 5, 2019. Pages 634-644.e3. https://www.sciencedirect.com/science/article/pii/S2451945619300352

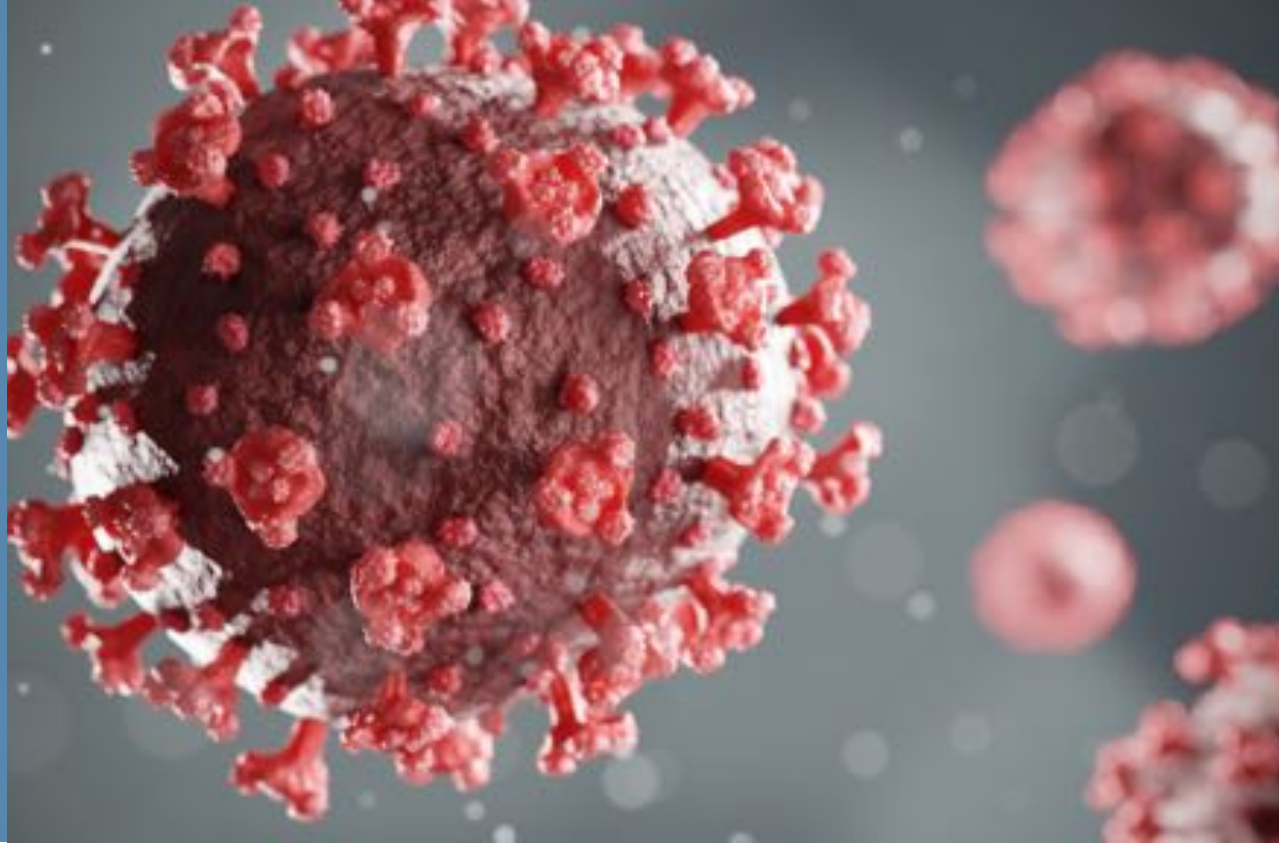
UPDATE: March 5, 2021: A change from previous versions of the guidance, known polysorbate allergy is no longer a contraindication to mRNA vaccinations; avoiding the Pfizer or the Moderna shot is merely a "recommendation." This is similar to people who have had anaphylactic reactions to eggs: for example, avoiding measles or influenza vaccines made with eggs is 'recommended' not a 'contraindication.'

Known polysorbate allergy remains a contraindication to Janssen COVID-19 vaccine.
REF: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

MOI #2 Anti-inflammatory macrophages, called M2, are inhibited by anti-spike -antibodies [Anti-S-Ab]

- Macrophages are a type of white blood cell that leave the blood stream and migrate into tissues when the tissues become infected. They engulf the pathogen and eliminates it.
- There are two primary types of macrophages: **type M1**, which are pro-inflammatory and are the first to arrive to "fight" the infection; and **type M2**, which are anti-inflammatory, which arrive as the "fire department" [to eliminate the cytokines] and the "clean-up crew" [to remove cellular debris as healing occurs.]
- The anti-S-antibodies [anti-S-Ab] skew the configuration toward cytokine producing macrophages (M1) by inhibiting the inflammation-resolving (M2) macrophages. This causes lung injury by promoting the uncontrolled release of proinflammatory cytokines, IL-8, IL-10, MCP1 and others.
- Animals that had been vaccinated and then contracted a SARS-CoV infection on re-exposure had an accumulation of pro-inflammatory macrophages (M1) and an **absence of wound-healing (M2) macrophages in the lungs.**
  - **REF**: Li Liu, et al. "Anti–spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. JCI Insight. 2019;4(4):e123158. https://doi.org/10.1172/jci.insight.123158





MOI #3 The damaging effects of the spike protein

- The spike protein can bind to the surface of the vaccine recipient's cells. This spike protein becomes a potential receptor for other more aggressive or more dangerous infectious agents.

  - **REF:** Classen JB. COVID-19 RNA Based Vaccines and the Risk of Prion Disease. Microbiol Infect Dis. 2021; 5(1): 1-3. https://carterheavyindustries.files.wordpress.com/2021/02/covid19-rna-based-vaccines-and-the-risk-of-prion-disease-1503.pdf

- SARS-CoV-2 is the only coronavirus with a prion-like domain found in the receptor-binding domain of the S1 region of the spike protein. SARS-CoV-2 demonstrates a 10- to 20-fold higher affinity for ACE2 receptor, their primary binding site, than SARS-CoV and other common coronaviruses.

  - **REF:** Tetz, G.; Tetz, V. SARS-CoV-2 Prion-Like Domains in Spike Proteins Enable Higher Affinity to ACE2. Preprints 2020, 2020030422 (doi: 10.20944/preprints202003.0422.v1)
    [Note: The SARS-CoV-2 virus is the only coronavirus with this receptor and affinity because SARS-CoV-2 was made/manufactured in a lab. The tighter the spike protein binds to the ACE receptor, the easier it is to enter the cell and replicate.]

- The SARS-CoV-2 spike protein may promote cardiovascular complications by binding to coronary (heart) blood vessels eliciting other cardiovascular diseases such as arrhythmias, coronary artery disease, hypertension, and stroke.

  - **REF:** Suzuki, Yuichiro J, and Sergiy G Gychka. "SARS-CoV-2 Spike Protein Elicits Cell Signaling in Human Host Cells: Implications for Possible Consequences of COVID-19 Vaccines." Vaccines. vol. 9,1 36. 11 Jan. 2021. https://www.mdpi.com/2076-393X/9/1/36/htm

MOI #4 The spike protein and risk of pulmonary artery hypertension (PAH)

- The SARS-CoV-2 spike protein can bind to ACE2 receptors and can promote pulmonary vascular wall thickening, that is a hallmark of pulmonary arterial hypertension (PAH).
- It is important to consider that the spike protein produced by the COVID-19 vaccines may do the same things.

NOTE: PAH is uniformly fatal. Even with currently available therapies, up to 70% die within 3yrs.

- **REF:** Suzuki, Yuichiro J, and Sergiy G Gychka. "SARS-CoV-2 Spike Protein Elicits Cell Signaling in Human Host Cells: Implications for Possible Consequences of COVID-19 Vaccines." Vaccines. vol. 9,1 36. 11 Jan. 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7827936/

MOI #5 The spike protein can bind to the ACE2 receptors on sperm and ovaries

- SARS-CoV-2 uses its spike protein to bind to angiotensin-converting enzyme 2 (ACE2) to enter human host cells. **Risk of infertility is possible but not yet proven.**
- ACE2 receptors are expressed on lung, intestine, and kidney tissues and also on the testis, sperm, ovaries, uterus, and vagina. The reproductive consequences of the spike protein – **whether from the virus or as a consequence of being injected with one of the COVID shots –** such as infertility and the risk of sexual transmission, are currently unknown. However, we should be alert to the possibility that there may be reproductive consequences of COVID-19 infection in males.

  - **REF:** Sheikh Zadeh Hesari F, et al. "Review of COVID-19 and male genital tract." Andrologia. 2021 Feb;53(1):e13914. https://pubmed.ncbi.nlm.nih.gov/33236375
  - **REF:** Morelli, Fabrício et al. "COVID-19 Infection in the Human Reproductive Tract of Men and Nonpregnant Women." The American journal of tropical medicine and hygiene, vol. 104,3 814–825. 18 Jan. 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7941816/

MOI #6 Neurological degeneration: Penetrating the Blood Brain Barrier (BBB)

- SARS-CoV-2 spike protein induces **loss of the BBB integrity** by triggering a pro-inflammatory response and upregulating enzymes (metalloproteinases - MMPs) in the barrier's cells.

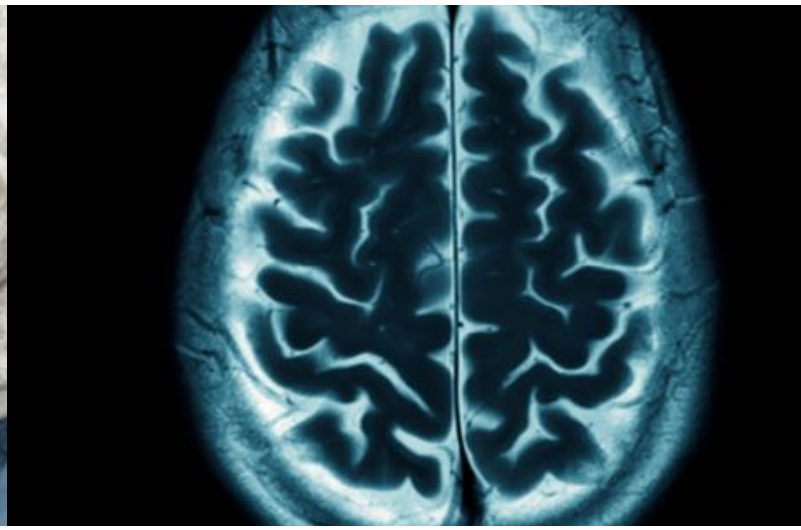
- Breaking down the BBB means many particles can pass directly into brain tissue. This explains the neurological conditions associated with the SARS-CoV-2 spike protein: **loss of smell, loss of taste, headache, seizures, uncontrolled tremors, etc.**
  - **REF:** Buzhdygana, Tetayna P, et al. "The SARS-CoV-2 spike protein alters barrier function in 2D static and 3D microfluidic in-vitro models of the human blood–brain barrier." Neurobiology of Disease. 146 (2020) 15113. https://www.sciencedirect.com/science/article/pii/S096999612030406X?via%3Dihub

This is a short, representative list of neurological disorders associated with loss of BBB integrity

- **Extrinsic:**
  - Multiple Sclerosis – autoimmune, infectious, traumatic initiation
  - Meningitis – bacterial, viral
  - Encephalitis – herpes, HIV, etc.

- **Intrinsic:**
  - Ischemia/hypoxia
  - Traumatic brain injury – edema, hemorrhage
  - Small vessel disease – hypertension, diabetes

  - **REF:** Rosenberg, Gary A. "Neurological diseases in relation to the blood-brain barrier." Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism vol. 32,7 (2012): 1139-51. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3390801/



MOI #7 Neurological degeneration: Amyotrophic Lateral Sclerosis

- At least 85 mutations in the *FUS* gene have been found to cause Amyotrophic Lateral Sclerosis (ALS), a condition characterized by progressive muscle weakness, loss of muscle mass, and inability to control movement.

- People with ALS caused by *FUS* gene mutations tend to develop the disease **at a younger age** and have a **decreased life expectancy.**

- At least 60 mutations in the TARDBP gene have been found to cause ALS. The TARDBP gene makes the *TDP-43 protein.* A change in a single amino acid in the *TDP-43 protein* can cause it to misfold and form clumps, leading to the inability to control movement.

- The amino acid sequence of the **Pfizer spike protein** may induce mutations of the *FUS* gene and the *TDP-43 protein,* leading to pathologic configurations and brain degeneration. Mutation, or damage, to the *FUS* gene and/or the *TDP-43 protein* has been **strongly associated with ALS.**

  - **REF:** Baloh RH. "How do the RNA-binding proteins TDP-43 and FUS relate to amyotrophic lateral sclerosis and frontotemporal degeneration, and to each other?" Current Opin Neurol. 2012 Dec;25(6):701-7. https://pubmed.ncbi.nlm.nih.gov/23041957/

  - REF: MedlinePlus, National Library of Medicine. TARDP gene https://medlineplus.gov/genetics/gene/tardbp/#conditions

MOI #8 Neurological degeneration: Frontotemporal Lobe Degeneration (FTLD)

The amino acid sequence of the **Pfizer spike protein** can lead to mutation and altered function of the TDP-43 protein, leading to neurodegenerative disease including a group of conditions known as frontotemporal lobe degeneration (FTLD), **a cluster of chronic degenerative neurological diseases.**

- **REF:** Baloh RH. "How do the RNA-binding proteins TDP-43 and FUS relate to amyotrophic lateral sclerosis and frontotemporal degeneration, and to each other?" Current Opin Neurol. 2012 Dec;25(6):701-7. https://pubmed.ncbi.nlm.nih.gov/23041957/

What is frontotemporal lobe degeneration? (FTLD)

Personality characteristics of FTLD include apathy, aspontaneity, inflexibility, disorganization, impulsivity, personal neglect, and poor judgment. FTLD is a collection of various forms of dementia. Defining features of Frontal Lobe Dementia (FLD) or Frontotemporal Lobe Degeneration (FTLD) include personality and behavioral disorders.

There are several subtypes thought to be associated with protein modification or pathological transformation of FDP-43 protein in the brain. Motor neuron degeneration often co-occurs with FTLD.

Subtypes: (various sources):

1. Behavioral variant Frontotemporal Dementia (bv-FTD): Early symptoms are dominated by **impairment in social behavior** and personal character. Patients say inappropriate things, ignore other peoples' feelings and have **difficulty in dealing with simple, daily situations.** Additional symptoms include a wide range of behaviors such as blurting out words and speech alterations. Binge eating is also common among bv-FTD patients.

2. Primary Progressive Aphasia (PPA): Persons with PPA experience a **gradual loss of their ability to speak, write, read, and/or understand what others are saying**. **This progresses to complete loss of both language and memory due to deterioration of brain tissue**. Eventually, almost all patients become mute and unable to understand spoken or written language, even if their behavior seems otherwise normal.

3. Progressive non-fluent/agrammatic aphasia: Persons with this form of FTLD have **difficulty forming words** but can retain the meaning of words. Grammar problems are a key feature, such as mixing up the order of words in a sentence.

4. Semantic variant Primary Progressive Aphasia (svPPA): This disorder is characterized by the **progressive, profound loss of meaning of words**. They can speak but say things that don't make sense.

They also demonstrate behavioral abnormalities due to the degeneration of the anterior temporal lobes.

5. Logopenic aphasia (also called progressive fluent aphasia): People with this subtype have difficulty finding the right words when they try to speak.

MOI #9 Risk of mutating the *FUS* gene and cancer

- The amino acid sequence of the **Pfizer spike protein** may induce the ***FUS gene*** to form pathologic conformations, that may lead to cancer.

- Mutations in the ***FUS gene*** are found in soft tissue sarcomas, which develop in bones or in soft tissues such as nerves or cartilage. FUS gene mutations have also been found in myxoid liposarcomas, which occur in fatty tissues of the body, and in cancer of the blood-forming cells in the bone marrow called acute myeloid leukemia (AML).

  - **REF:** FUS gene, MedlinePlus, National Library of Medicine. https://medlineplus.gov/genetics/gene/fus/#references

MOI #10 Adenoviruses and the risk of cancer

The currently authorized Johnson and Johnson injection is made from Ad26.COV-2.S shell, a human adenovirus first isolated in 1956 from an anal specimen obtained from a 9-month old male infant (https://doi.org/10.1016/j.vaccine.2020.09.018)

The Oxford/AstraZeneca vaccine uses ChAdOx1, which is an adenovirus strain which normally infects **chimpanzees.**

- More than 100 serologically distinct types of adenovirus have been identified, including 49 types that infect humans.

- Most of the **adenovirus-induced tumors,** tumor cell lines, and transformed cell lines carry one or several copies of the viral genome integrated into the chromosomes.

"Oncogenes in adenovirus-induced tumor or transformed cells have received surprisingly little attention."

- Adenoviruses are excellent antigens. However, viral vaccines usually have not included them because **adenoviruses are involved in tumorigenesis in animals and in cell culture.**

  - **REF:** Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 67 Adenoviruses by Walter Loeffler. https://www.ncbi.nlm.nih.gov/books/NBK8503/

- **Ad26.COV2.S used in the J&J shot** has been designed to deliver a transgene encoding to create the SARS-CoV-2 the spike protein. Ad26 vector-based vaccines are manufactured using **PER.C6 cell line,** from retina cells of an **aborted human fetus.**

  - **REF:** Janssen BioNTech, Inc. COVID-19 Vaccine Ad26.COV2.S VAC31518 (JNJ-78436735) Briefing document. VRBPAC meeting. Feb. 26, 2021. pg. 12 https://www.fda.gov/media/146219/download#page=96

- **Transgenics refers to the movement of genes between organisms of different species.** The transferred gene is called a **transgene**. Transgenes can alter the phenotype [genetics] of the receiver. A transgene can be used by the cell to produce a new protein that the cell could not make before.

  - **REF:** How Genetic Engineering Can Be Used To Produce Human Insulin https://diabetestalk.net/insulin/how-genetic-engineering-can-be-used-to-produce-human-insulin

- The transgene can randomly insert into the genome. When a transgene incorporates into the host's DNA, it can lead to **chromosome instability.**

  - **REF:** Davis, Jennifer, et al. Lost in Transgenesis: A User's Guide for Genetically Manipulating the Mouse in Cardiac Research. Circulation Research. 2012; 11:761-777. https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.111.262717

MOI #11 The damaging effects of the anti-S-antibody

- There was a direct, positive correlation between the level of anti-spike antibody in the blood stream and the **degree of serious lung injury** in the Macaque monkeys.

- The lung tissue had evidence of **diffuse alveolar damage (DAD),** with various degrees of exudate (pus-like fluid) and hemorrhage (bleeding).

- **The anti-spike antibody caused severe acute lung injury (ALI) when the animals were re-infected by suppressing the inflammation-resolving M2 macrophages.**

  - **REF:** Li Liu, et al. "Anti–spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. JCI Insight. 2019;4(4):e123158. https://doi.org/10.1172/jci.insight.123158

- In severe cases of COVID illness, multiple organs can be inflamed, including the lung, heart, liver, and kidney. There can also be inflammation in the blood and nervous system, leading to multi-organ failure. **SARS-CoV-2 can directly invade the organ's cells through the ACE2 receptors on and within these organs.**

- In addition, activation of the complement system, **cytokine storm**, dysregulated immune responses, coagulation dysfunction, and infiltration of inflammatory cells in SARS-CoV-2 infection can also lead to **multi-organ failure i**n these patients.

  - **REF:** Mokhtari, Tahmineh et al. "COVID-19 and multiorgan failure: A narrative review on potential mechanisms." Journal of molecular histology vol. 51,6 (2020): 613-628. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7533045/

- **SARS-Cov-2 antibodies to the spike protein and the surface nucleoprotein cross-reacted with 28 out of 55 tissue types tested.** The reactions occurred in gut and barrier proteins, gastrointestinal system cells, the mitochondria, and in the tissues of the thyroid, nervous system, heart, joints, skin, muscle, and liver.

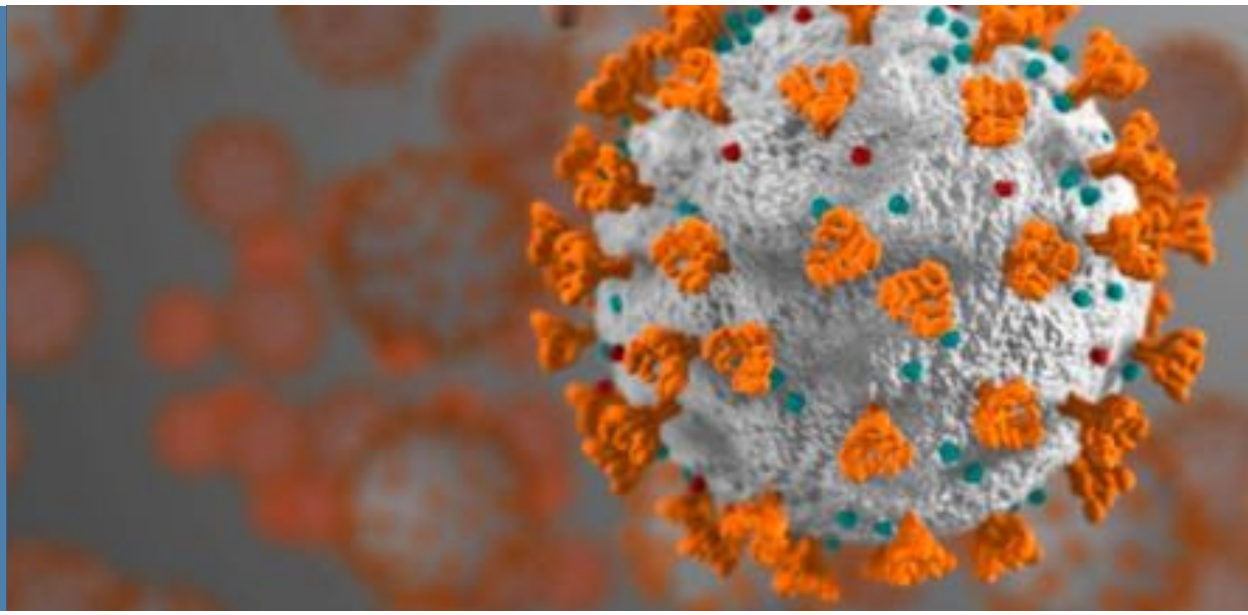
  - **REF:** Vojdani, Aristo, et al. "Reaction of Human Monoclonal Antibodies to SARS-CoV-2 Proteins With Tissue Antigens: Implications for Autoimmune Diseases." Front. Immunol., 19 January 2021 https://doi.org/10.3389/fimmu.2020.617089

MOI #12 The concept called 'original antigenic sin' [See Diagram #4 below]

Let's use an example to explain "original antigenic sin"

- When a person is exposed to a coronavirus, the immune system responds with the release of a very specific IgG antibody formed against this FIRST coronavirus.
- When later exposed to the SARS-CoV-2 virus, B-cells "remember" the first coronavirus exposure, even if it was many years ago.
- The B-cells produce "memory antibodies," not antibodies to the SARS-CoV-2 virus. These antibodies are inadequate and are referred to as non-neutralizing, non-binding antibodies.
- They do not protect against the new "invader" but instead, enhance the infection. The person can become very ill through a phenomenon called antibody dependent enhancement (ADE). ADE elicits sustained inflammation, lymphopenia, and sometimes, cytokine storm. All of these have been associated with coronavirus severe illness and death.

  - **REF**: Firez, Walter Fierz and Walz, Brigitte Walz. "Antibody Dependent Enhancement Due to Original Antigenic Sin and the Development of SARS" Front. Immunol., 05 June 2020. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01120/full
  - **REF**: Monto, Arnold S et al. "The Doctrine of Original Antigenic Sin: Separating Good from Evil." The Journal of Infectious Diseases. Vol. 215,12 (2017): 1782-1788. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5853211/#CIT0002
  - **REF**: Vatti A, et al. "Original antigenic sin: A comprehensive review." J Autoimmune. 2017 Sep;83:12-21. https://pubmed.ncbi.nlm.nih.gov/28479213/



MOI #13 Increased risk of COVID illness and COVID-related death after an influenza vaccines

- Receiving an influenza vaccination may increase the risk of illness by other respiratory viruses, a phenomenon known as **viral interference**. Viral interference has been significantly associated with coronaviruses and human metapneumoviruses.

- Examining infection caused by non-influenza viruses showed **the odds of contracting coronavirus in individuals who have received an influenza vaccine were significantly higher when compared to unvaccinated individuals.**

- The odds ratio (the association between an exposure and an outcome) of 1.36. In other words, **the vaccinated were 36% more likely to get coronavirus illness**.

  - **REF**: Wolf, Greg G. "Influenza vaccination and respiratory virus interference among Department of Defense personnel during the 2017–2018 influenza season." Vaccine, Volume 38, Issue 2, 2020, Pages 350-354. https://www.sciencedirect.com/science/article/pii/S0264410X19313647?via%3Dihub

- For the US and 26 European countries assessed, the results indicated that COVID-19 deaths per million inhabitants [DPMI] and the COVID-19 case fatality ratio [CFR] were **positively and statistically significantly associated with influenza vaccination rate,** especially in people ≥65 years old. [i.e. COVID deaths were positively associated with flu shots].

  - **REF**: Wehenkel C. 2020. Positive association between COVID-19 deaths and influenza vaccination rates in elderly people worldwide. PeerJ 8:e10112 DOI 10.7717/peerj.10112. https://peerj.com/articles/10112/

MOI #14 High (strong) antibody responses to both COVID illness and to the shots results in prolonged illness and worse outcomes

- When an mRNA shot (Pfizer or Moderna) is given to a person who recovered from a COVID infection, small-scale studies have shown that a single mRNA injection rapidly boosts antibody titers (concentrations) to very high levels.

  - **REF**: Moore, John. "Approaches for Optimal Use of Different COVID-19 Vaccines: Issues of Viral Variants and Vaccine Efficacy." JAMA. Published online March 4, 2021. https://jamanetwork.com/journals/jama/fullarticle/2777390

- **A robust antibody response is associated with delayed viral clearance and increased severity of infection**. Patients with a strong antibody response had only 9% of virus clearance at seven days, whereas 57% of people who had a weak antibody cleared the virus in seven days.

- Further, if IgM antibody was released at the same time the person was developing a high IgG antibody response, the person had a much more severe infection.

  - **REF**: Fierz, Walter and Walz, Brigitte Walz. "Antibody Dependent Enhancement Due to Original Antigenic Sin and the Development of SARS." Front. Immunol., 05 June 2020. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01120/full

MOI #15 COVID shots lead to enlarged lymph nodes that may have long term ramifications

- Efforts are being made to enhance the efficacy of COVID shots by using adjuvants, particularly adjuvants targeting the Toll-like receptors (TLRs).

mRNA can be used to create nearly any protein. Moderna's patent describes an mRNA for the production of an experimental adjuvant: **flagellin**. Moderna's patent lists dozens of possible mRNAs targeted to be in future shots, referring to them as "some embodiments"

- The administration of flagellin or flagellin-based vaccines has been shown to rapidly achieve a **higher concentration in draining lymph nodes**.

Is mRNA coded for flagellin already in the current shots?

- **Mammogram warning**: Lymphadenopathy was detected unilaterally in the arm and neck within 2-4 days of vaccination and lasted on average 10 days on exam. The duration of subclinical adenopathy on mammography is likely to be greater and is likely to last longer.

RECOMMENDATION: Schedule screening exams prior to the first dose of a COVID-19 vaccination or 4-6 weeks following the second dose of a COVID-19 vaccination.

- **REF**: Society for Breast Imaging: Recommendations for the Management of Axillary Adenopathy in Patients with Recent COVID-19 Vaccination. https://www.sbi-online.org/Portals/0/Position Statements/2021/SBI-recommendations-for-managing-axillary-adenopathy-post-COVID-vaccination.pdf

MOI #16 Widespread use of COVID shots results in non-neutralizing antibodies and can lead to virulent mutant viral serotypes (strains)

- The combination of high viral replication rate in individuals who also produce suboptimal, non-neutralizing antibodies creates the exact environment in which **resistant viruses are likely to emerge and spread.**

  - **REF:** Moore, John. "Approaches for Optimal Use of Different COVID-19 Vaccines: Issues of Viral Variants and Vaccine Efficacy." JAMA. Published online March 4, 2021. https://jamanetwork.com/journals/jama/fullarticle/2777390

- The antibody response to mRNA shots is higher than titers seen in convalescent (recovering) individuals. This results in a high ratio of **non-neutralizing antibodies.**

  - **REF:** Amana, Fatima et al . "The plasmablast response to SARS-CoV-2 mRNA vaccination is dominated by non-neutralizing antibodies that target both the NTD and the RBD." medRxiv 2021.03.07.21253098. https://www.medrxiv.org/content/10.1101/2021.03.07.21253098v1.full

MOI #17 Antibody Dependent Enhancement (ADE) upon re-exposure to circulating coronavirus causes extensive illness

Because SARS-CoV and SARS-CoV-2 viruses have approximately 78-85% genetic overlap, it is presumed a reaction would be similar in both.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7827936/

- There is a growing concern for individuals who have received a COVID shot and the pathology (illness) that will develop when these individuals are re-exposed to common coronaviruses or the SARS-CoV-2 virus.

  - **All test animals had autoimmune injury to their lungs after a re-exposure.**
  - Exposure to SARS-CoV is associated with prominent inflammatory infiltrates (pneumonia) characterized by a **predominant eosinophilic (allergic) component.**

- **Vaccinated macaques monkeys:** Lung tissue revealed **acute diffuse alveolar (ADA)** injury with various degrees of severity at 7 and 35-days post-infection. Wound healing was blocked by **anti-S-IgG antibodies,** resulting in prolonged macrophage activity and **promotion of severe lung injury.**

- **Unvaccinated macaques:** Lung tissue revealed **only minor to moderate inflammation.** Alveolar monocytes/macrophages assume a wound-healing function ***as early as two days*** after onset of infection in macaques who were unvaccinated.

- **REF:** Li Liu, et al. “Anti–spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. JCI Insight. 2019;4(4):e123158. https://doi.org/10.1172/jci.insight.123158

- **REF:** Jason A.Tetro. “Is COVID-19 receiving ADE from other coronaviruses?” Microbes and Infection Vol 22, Issue 2, March 2020, Pages 72-73. https://www.sciencedirect.com/science/article/abs/pii/S1286457920300344?via%3Dihub

MOI #18 Injecting raw genetic material can induce anti-DNA antibodies. DNA can integrate into the human DNA.

- ***Both the Johnson/Johnson shot and the AstraZeneca shot are designed to deliver double-stranded DNA (ds-DNA) fragments to the cytoplasm of the cells called a transgene.***

- **A transgene** is a segment of DNA used to introduce genes from one organism to another organism. In this instance, the DNA is inserted into the recipient’s DNA.

- It is presumed that the DNA is translated into mRNA, leading to the production of the spike protein and anti-spike-antibody. **The use of a transgene is considered to be a genetic engineering technique.**

    - **REF:** Dr. Mae Wan-Ho. "Transgenic Lines Unstable hence Illegal and Ineligible for Protection." https://www.i-sis.org.uk/transgenicLinesUnstable2.php

- **Induction of anti-DNA antibodies**
    - Stray DNA, similar to the spike proteins, can function as a hapten by binding to the surface of organs.
    - Haptens alone do not stimulate an immune response, but **when bound to a protein**, they can lead to autoimmune reactions.

Integration of DNA into host genome

- The segment of DNA can be integrated into the human genome, which may have devastating consequences by inducing mutations in essential structural genes or in causing mutations that can lead to cancer.

    - **REF:** Bona, Constantin A, and Bot, Adrian. “Genetic Immunization.” Kluwer Academic /Plenum Publishers. 2000. Pg. 9. [TEXTBOOK]

MOI #19 Antibodies to dsDNA can lead to a long list of autoimmune disorders

- **anti-dsDNA antibody** is highly specific for **Systemic Lupus Erythematosus (SLE).**
- **anti-dsDNA antibodies** were also detected in the following conditions: other autoimmune diseases, other rheumatological disorders, malignancies, infections, autoimmune hepatitis and sarcoidosis.

  - **REF:** Attar SM, Koshak EA. Medical conditions associated with a positive anti-double-stranded deoxyribonucleic acid. Saudi Med J. 2010 Jul;31(7):781-7. https://www.academia.edu/23304303/Medical_conditions_associated_with_a_positive_anti_double_stranded_deoxyribonucleic_acid

MOI #20 AstraZeneca: Potentially deadly blood clots called Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT)

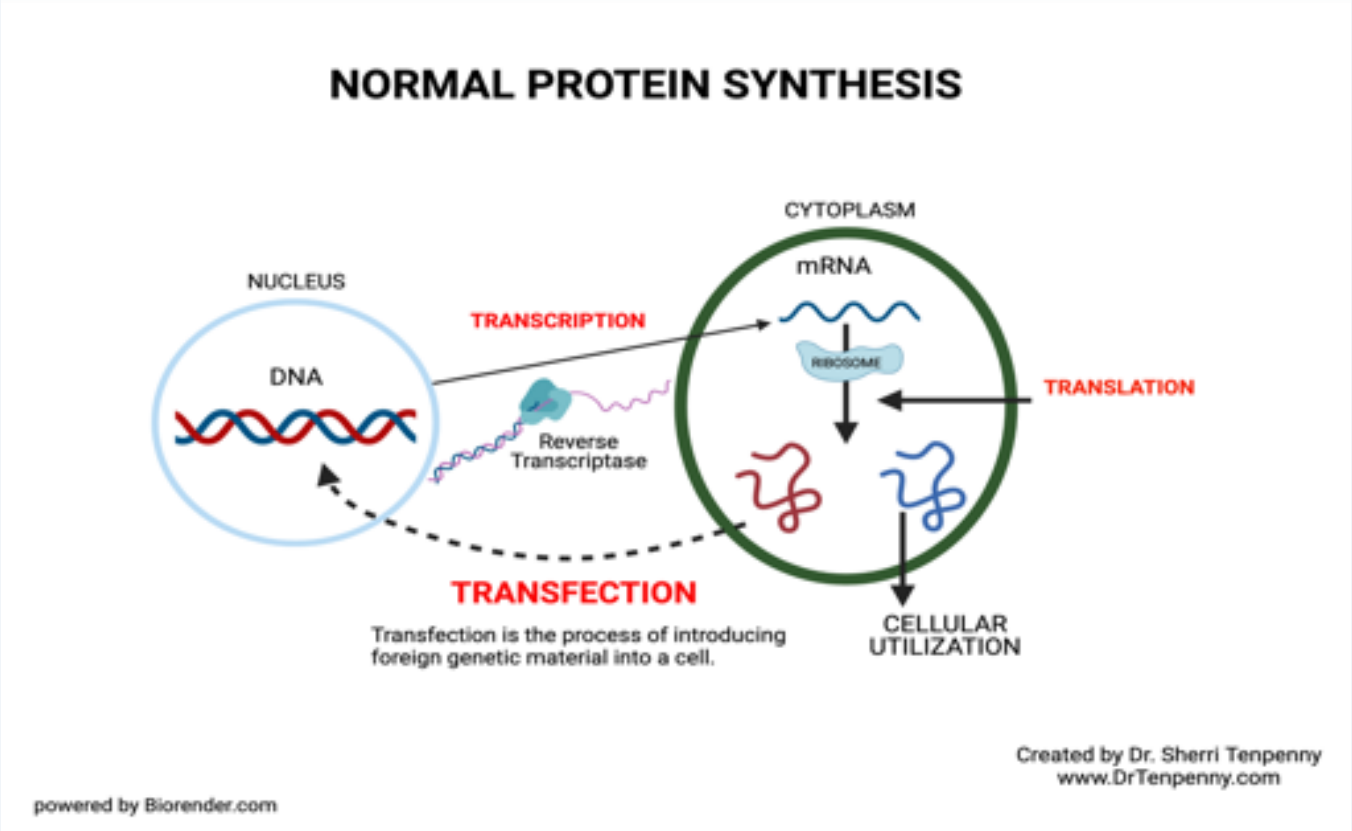
- VIPIT is a newly reported condition found after the injection of the AstraZeneca COVID19 shot. The shot may be associated with blood clots and thrombocytopenia (low levels of blood platelets).
- Clots have formed in extremities and in veins draining blood from the brain. Called a cerebral venous sinus thrombosis (CVST), when a blood clot forms in the brain's venous sinuses, it prevents blood from draining out of the brain. As a result, blood cells may break and leak blood into the brain tissues, forming a hemorrhage.
- Based on available information, the case fatality of VIPIT is approximately 40%. The exact mechanism by which the AstraZeneca shot triggers VIPIT is still under investigation.
- **KEY:** Any patient with unusual symptoms following the injection (4 to 20 days) should be assessed by a health care provider. ***Symptoms associated with VIPIT include:*** persistent and severe headache; focal neurological symptoms (including blurred vision); shortness of breath; abdominal or chest pain; swelling and redness in a limb; or pale color and coldness in a limb.

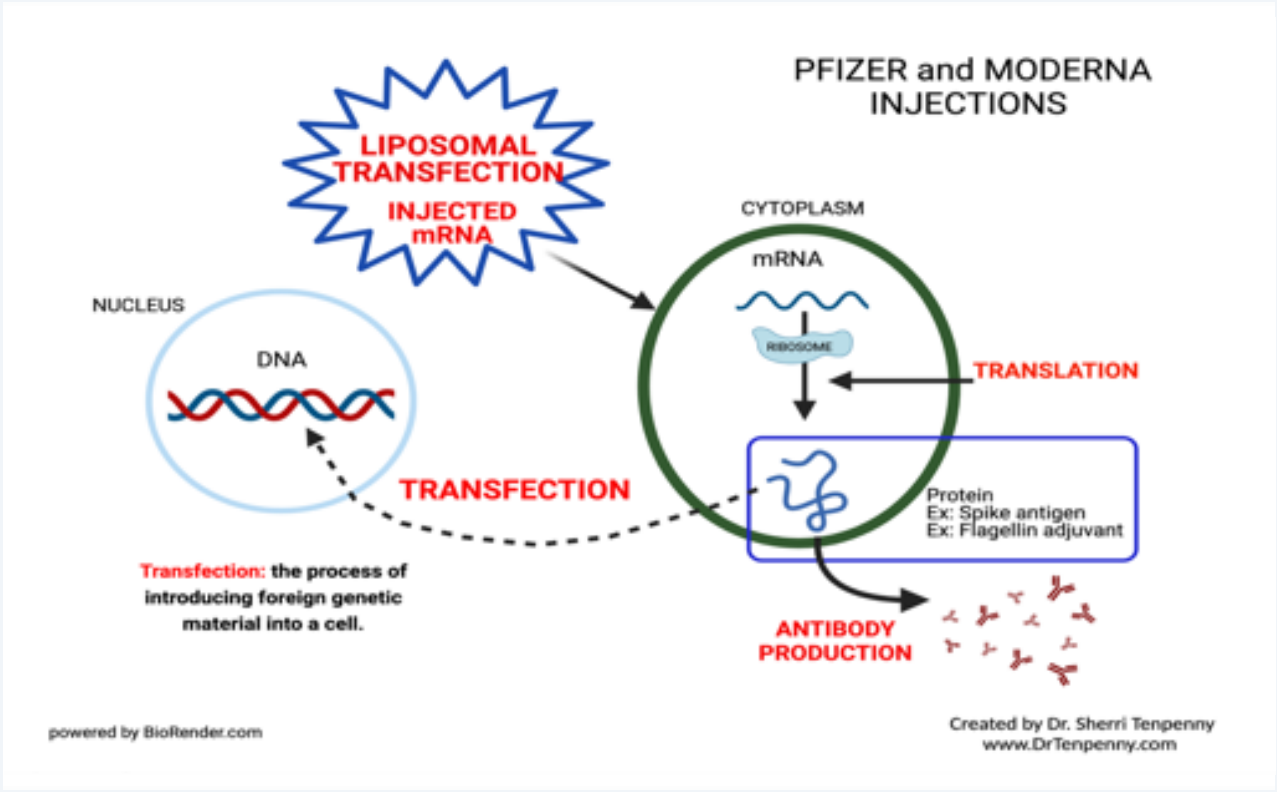
  - **REF:** COVID-19 Vaccine AstraZeneca: benefits still outweigh the risks despite possible link to rare blood clots with low blood platelets https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-benefits-still-outweigh-risks-despite-possible-link-rare-blood-clots
  - **REF:** Pai M, et al. "Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) following AstraZeneca COVID-19 vaccination." Version 1.0. Ontario COVID-19 Science Advisory Table. 2021 Mar 26. https://doi.org/10.47326/ocsat.2021.02.17.1.0

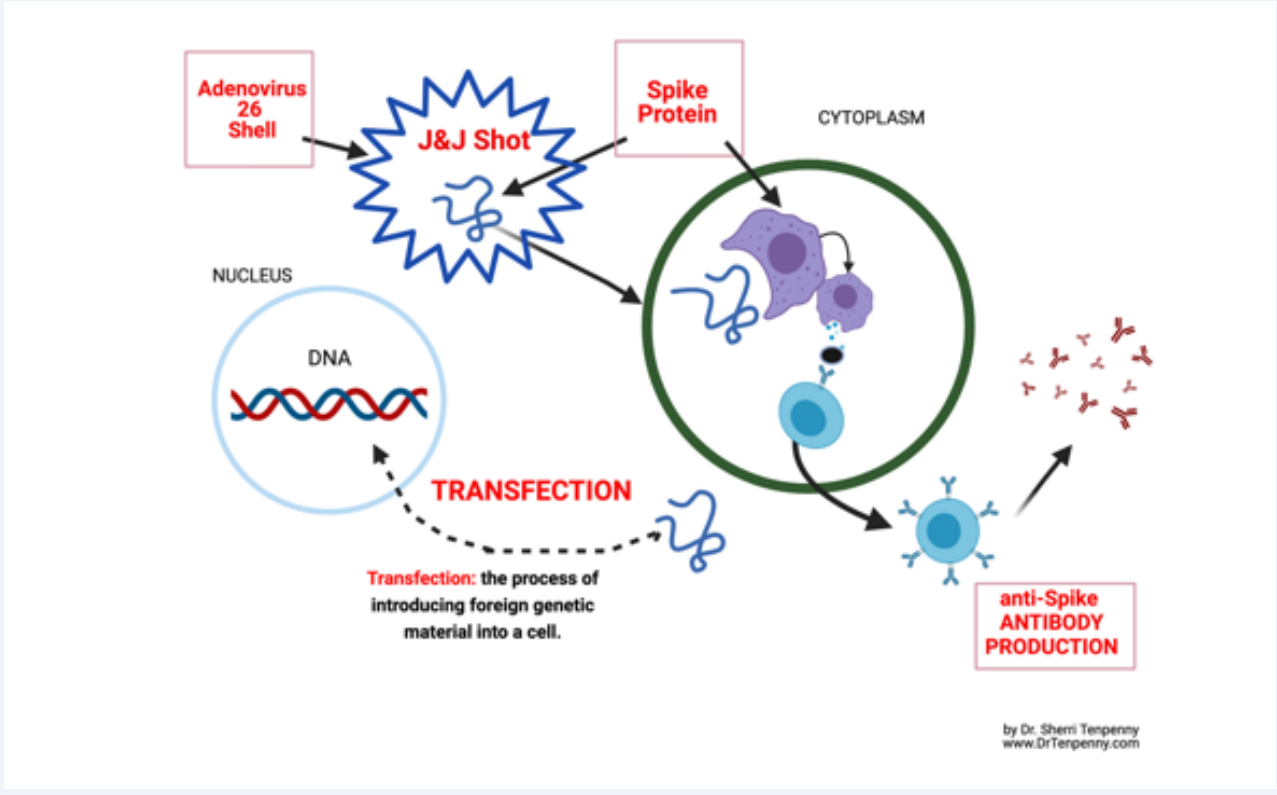
Outcomes of Animal Study

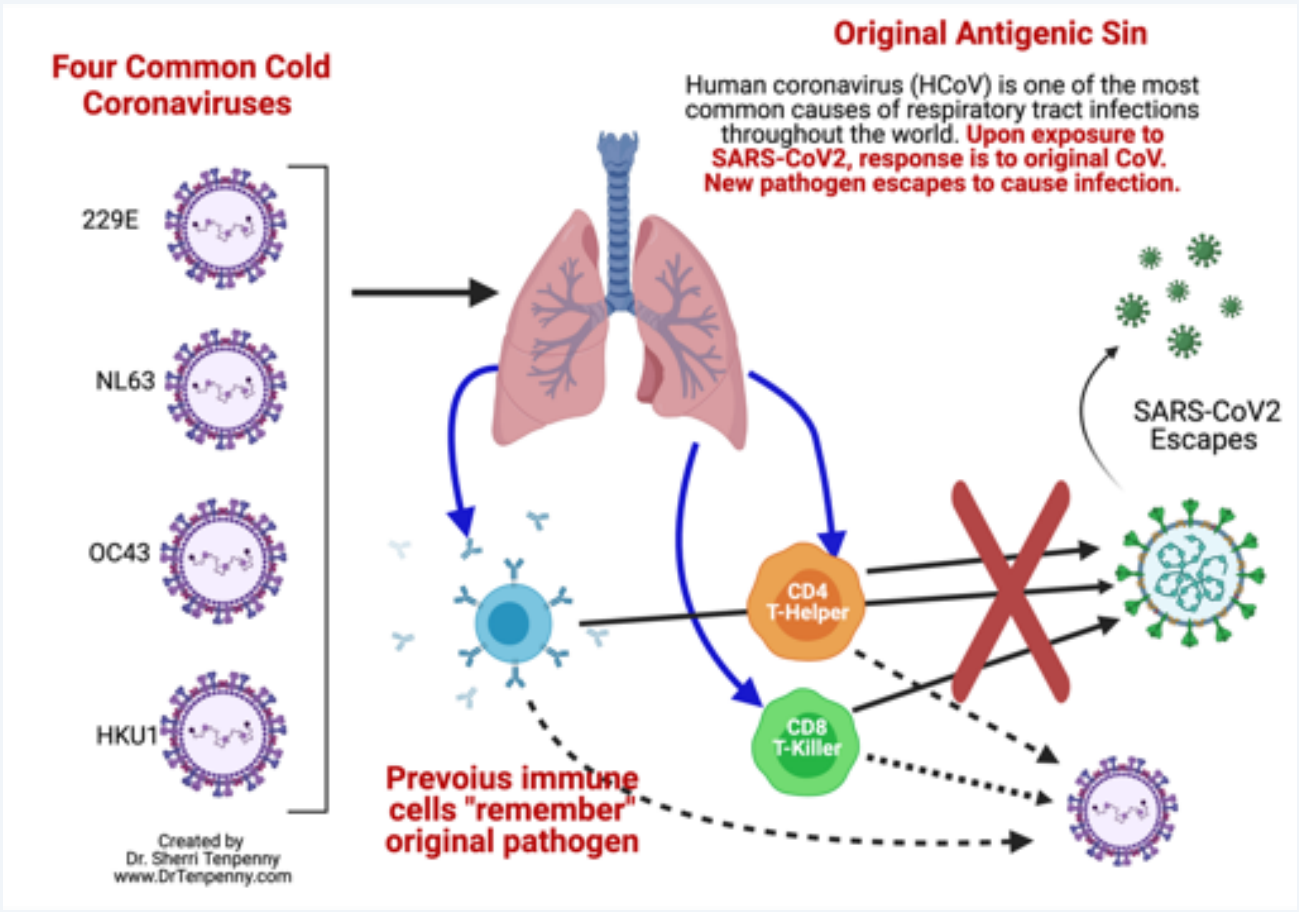
"An inactivated vaccine preparation that does not induce this result in mice, ferrets and nonhuman primates has not been reported." [translation: vaccine induces damage to lungs after re-exposure in all animals tested – mice, ferrets, monkeys]. When challenged, vaccinated mice developed Th2-type immunopathology suggesting hypersensitivity to SARS-CoV components. **Caution in proceeding to application of a SARS-CoV vaccine in humans is indicated."**

- **REF:** Tseng C-T, et al. "Immunization with SARS Coronavirus Vaccines Leads to Pulmonary Immunopathology on Challenge with the SARS Virus." PLoS ONE 7(4):e35421. 2012. doi:10.1371/journal.pone.0035421 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0035421




PFIZER and MODERNA
INJECTIONS
LIPOSOMAL
TRANSFECTION
INJECTED
mRNA
CYTOPLASM
mRNA
RIBOSOME
NUCLEUS
DNA
TRANSLATION
TRANSFECTION
Protein
Ex: Spike antigen
Ex: Flagellin adjuvant
Transfection: the process of
introducing foreign genetic
material into a cell.
ANTIBODY
PRODUCTION
powered by BioRender.com
Created by Dr. Sherri Tenpenny
www.DrTenpenny.com


Adenovirus
26
Shell
J&J Shot
Spike
Protein
CYTOPLASM
NUCLEUS
DNA
TRANSFECTION
Transfection: the process of
introducing foreign genetic
material into a cell.
anti-Spike
ANTIBODY
PRODUCTION
by Dr. Sherri Tenpenny
www.DrTenpenny.com



ALL AVAILABLE AT DRTENPENNY.COM

Bi-Annual Boot Camp: MasteringVaccineInfo.com
Advanced Education: VaccineU.com
Membership: THE TENPENNY FILES, PREMIUM
Inspiration: HappyHourWithDrT.blogspot.com
Research: TenpennyResearchLibrary.com
Pod Cast: TenpennyFiles.podbeam.com
Activism: Vaxxter.com
Social Media: Instagram, Twitter, GAB, Uniting.Zone, Disseminate.TV