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## **TRANSCRIPT - GR 02 11 22 "Vaccines: When you should be hesitant. Vaccine precautions and**

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### **UVA IM Chiefs**

00:18:56 Alright, everyone, welcome to grand rounds, we will go ahead and kind of get started so today's grand rounds will be given by Dr Michael no Nelson.

- 00:19:08 Our division Chief of asthma allergy and immunology Dr Nelson graduated from Princeton in 1985 with his Bachelor of Arts degree in chemistry and then came to uva to complete his md and PhD.
- 00:19:22 After completing his internship in internal medicine at uva Dr Nelson completed his internal medicine residency at the Eisenhower army medical Center in Fort Gordon Georgia.
- 00:19:32 And then completed sub specialty training, allergy, and immunology at Walter reed army medical Center.
- 00:19:39 Dr Nelson has had an illustrious career in both the armed services and in the civilian medical community having risen to the rank of Colonel in the US army and is the current President of the American Board of allergy and immunology.
- 00:19:53 Dr Nelson joined uva as a professor of medicine and division chief in 2020 and brought with him a diverse set of interest within medical education and his sub specialty and also an incredible array of leadership roles in the medical field.
- 00:20:09 Dr Nelson is a former fellowship director professor of medicine and pediatrics at the uniformed services University of the health sciences.
- 00:20:17 And chief consultant to the United States army surgeon general among other positions in the civilian and military world.
- 00:20:25 He has authored over 50 peer reviewed publications abstracts and book chapters and is frequently giving updates for the major professional societies and allergy, and I mean algae.
- 00:20:36 For all his service, he was awarded both the distinguished service award from the American Board of medical specialties and the Legion of merit medal from the US army medical corp in 2019.
- 00:20:48 Today, Dr Nelson will be giving a very timely update on vaccine adverse effects contraindications and precautions with that i'll give it over to Dr Nelson.

### **Mike Nelson**

00:21:00 wow, thank you for that very flattering introduction and frankly I don't even recognize that person you just described appreciate it very much and I appreciate the organizers for giving me the opportunity to present to you in this great forum of grand rounds at the Department of medicine.

- 00:21:18 It is great to be back at uva since those days in Medical School, a lot has changed.

- 00:21:25A little greatly disappointed that I haven't been able to get out about and see old friends and meet new ones do some of the pandemic.
- 00:21:32Precautions but, hopefully in the coming year, I will get to see each and every one of you in the halls in collaboration to advance the health of patients and science.
- 00:21:43So yes, there have been great presentations on vaccine hesitancy in the setting of code 19 vaccine.
- 00:21:51I don't want to reiterate some of those tenants I'll touch on a few of them, but I would like to continue the conversation of vaccines.
- 00:22:00And to remind us that there are indeed some reasons, when we should hesitate before giving a vaccination.
- 00:22:07Note I say hesitate, because in most instances, there are very few absolute contraindications and reasons not to vaccinate so march through.
- 00:22:17What I like to say is a high overview of the vaccine precautions and adverse events and considerations, so that we can be honest with our patients and prevent devastating disease so with that let's launch in.
- 00:22:32today's talk.
- 00:22:36So disclosures none they're really relevant to this talk specifically I am the site pih coast sponsored clinical study that i'll talk about just a moment.
- 00:22:48i'm also in the process of establishing some clinical trials for with some emerging and you know modulator treatments with Sanofi and Astrid Seneca.
- 00:22:57you've heard my various leadership positions as part of the introduction so it's important to know that when I do express opinion they really are mine not any of those organizations, of which I represent in other capacities.
- 00:23:11So here are today's objectives will review common contraindications and precautions for some of the routine scheduled vaccines so also touch on some of the rare adverse events they really have a scratching our head sometimes as to.
- 00:23:26What is going on with some of these vaccines and what are the risk factors, some of these rare adverse events that really do get in the way of vaccinating everyone.
- 00:23:39I gotta tell you as an allergist and you know just it does indeed warm my heart failure here literally everybody talking about backseat it's um it's fantastic, it was a foregone conclusion.
- 00:23:51In the past, but now everybody is talking about vaccines and to me that's a good thing.
- 00:23:57So you see here 50 years of vaccine citations and public indeed there has been an explosion, with respect to publications.
- 00:24:06And there is also an explosion of conversation in the streets amongst our patients and civilians itself.
- 00:24:13it's my hope that this new energy is indeed a reset for vaccine health and tremendous power, it has to prevent disease and reduce morbidity, mortality over time for both common and as we've seen in the last couple of years, not so common to see.
- 00:24:31Some why there's talk where there's conversation there's certainly misinformation and personal opinion so that's the call Darren for us as physicians is to arm ourselves.
- 00:24:42With the latest evidence based information so that we can make decisions with our patients and maximize health and prevention of disease.

- 00:24:53I thought I'd seen the peak of public passion over vaccinations a couple of decades ago with the mmr and time aerosol allergy with concerns for a autism.
- 00:25:02And haven't been immersed in the Department of Defense seeing the rollout of the anthrax smallpox vaccines.
- 00:25:09boy was Iraq, as you can see in this picture here on the slide personal and political overtures really a time to overshadow the science of vaccines, so I think we're indeed.
- 00:25:21in need of a reset where we can rebuild trust with clear communication of the risk of benefits for all maxine.
- 00:25:29Just imagine, where we wouldn't be as a society without vaccines, preventing these devastating diseases, each and every day So yes, I am a.
- 00:25:39Temporary voting Member on the FDA advisory committee for vaccines it's a tremendous honor and opportunity to be amongst colleagues to look at.
- 00:25:48novel pivotal data help make decisions on which vaccines are being brought to the table certainly we've been busy as a committee, with the coven 19 vaccines.
- 00:25:58And the public outcry has been tremendous so I submitted this talk for CME approval last week and it counted about 3200 personal emails right in my inbox so just this morning I rechecked and sure enough it's over 11,000.
- 00:26:13There are a lot of passionate people out here need the latest and greatest evidence with respective accidents, not just coven 19 but for all of them, I think we can do our part I stay up to date with the greatest knowledge of what the true adverse effects and risk are for these vaccines.
- 00:26:34So there are multiple organizations who have recognized that the communication of vaccine adverse effects and the conversation in the leg press.
- 00:26:46has been problematic and that some of our own providers may have strayed outside of the standard of care for the provision of vaccines and treatments for code in it.
- 00:26:57So here we see statements from the American Board of medical specialties and one I author for the American Board of allergy immunology and there are several others.
- 00:27:06who have really called arms the physicians who are providing care that we really do stick to evidence based treatments and recommendations, and I think we can do that in forums like this by.
- 00:27:19Making sure we're knowledgeable the latest and greatest with respect to data.
- 00:27:24So here's what I would like to cover with that lead in over the next 4045 minutes or So hopefully we'll have plenty of time for questions at the at the end.
- 00:27:34we'll begin by looking at really what's in the eight and individual vaccine dogs it's, not a single component, as you might imagine there are several acceptance and other components that can really be the source of allergic reactions.
- 00:27:49So I'll begin with a case, this is a true and true case I have is a fellow back at Walter reed a healthy four month old came in with the history of experiencing highs any irritability.
- 00:27:5910 minutes after receiving for vaccines and common scenario vaccines are given in combination, most of the time, these days, due to the complexity of the schedule.
- 00:28:10So what do you do here's the theoretical part this kid is avoided vaccines for an extended period of time gets admitted to our school of medicine could have happened didn't really but.

- 00:28:21 We still have patients who certainly avoid vaccines, after a single reaction and said, you know I've had a reaction.
- 00:28:28 Not doing anymore and end up going for years without having one, so the question to you is what would you do as a primary care provider.
- 00:28:37 The program director trying to get the student in your program or the institutional health leaders so we'll pause on that one, and then you can think about it and what's now launch into a review of some of the components of things that can cause out.
- 00:28:53 Here is the spectrum of allergic reactions, we see to drugs and vaccines, they really do overlap significantly on the top are the classic iga mediated allergic reactions, beginning with cutaneous only wheal and player reactions.
- 00:29:09 And then progressing to the more multi system anaphylaxis and life threatening reactions that can occur, yes, like starting reactions can occur with vaccinations and.
- 00:29:20 As you've heard with coven 19 early in its initial rollout on anaphylaxis signal, that is since we're.
- 00:29:27 On the bottom of the slide are not it immediately reactions again, beginning with local reactions, they can also become very, very severe, including Steven Johnson syndrome T, yes, there are six reports and there's a coven 19 vaccines, causing as J s amp T, so it does a curl rare very thing.
- 00:29:51 So I point this out because yes there's a spectrum of reactions that can occur, but patients often come in stating they have an allergy to vaccine and it can be any one of these.
- 00:30:04 So the challenge for physicians and primary care providers to decipher what that allergy to a vaccine really means for that individual patient where on the spectrum is it and what.
- 00:30:17 Individual rest is this particular location have for future vaccinations and doesn't really require additional testing to sort out what's really going on.
- 00:30:29 Vaccines come in a variety of platforms for their active component.
- 00:30:35 classics being the killer in it inactive forms of vaccines toxins and the live attenuated vaccines real literally around for a century newer platforms are obviously garnering a lot of attention they include the RNA vaccines and the viral vector effects.
- 00:30:52 Although these two vaccines for coven 19 or these two platforms are touted as new they're really not so you can see my mouse or not, but.
- 00:31:05 The Mr and a platform really had been in development for over 10 years there already was an FDA approved Mr in a vaccine on the market for this rare disease, they amyloidosis.
- 00:31:16 Even before the first patient was ever infected with stars cody to.
- 00:31:21 Similarly for the viral vector vaccines J and J being the coat the cynical known here in the US, there was already and involved vaccine have been approved with this technology.
- 00:31:34 So the platforms have been tried and true and tested and there are some specific risk associated with each of these platforms, that will get into a little bit, but the next series of slides.
- 00:31:47 So let's look a little bit at some of the immune mechanisms underlying that spectrum of hypersensitivity reactions I just talked about.
- 00:31:56 begin with the antibody reactions on the left, you see, in a classic hives and an ID mediate cutaneous reaction.

- 00:32:06 The causative factors for those are most often the acceptance and you see Here are some examples of a gelatin and, yes, even alpha gout can serve as a potential allergen for individuals evoking iga mediated reactions.
- 00:32:21 And then we also see I GG can be problematic for folks as well the classic large local reaction or artists, I mean complex deposition shown here.
- 00:32:33 Other off target effects are no more delayed fashion and mediated by our cellular immunity so here in the T cell mediated reactions that we often see.
- 00:32:43 classic contact hypersensitivity in the way of metals that are sometimes have included in taxi preparations.
- 00:32:52 And some of them were delayed cellular immune response reactions like we've seen with smallpox and the development of myopia titus.
- 00:32:59 centrally and neuropathic events occur with a mixed lymphocytes reactions that can lead to devastating effects So these are all in award delayed fashion and they all have some predisposing risk factors, be the genetic or others.
- 00:33:15 That we're still trying to sort out to really understand what individual risk is for these types of reactions.
- 00:33:22 And it is also important to remind all of ourselves, the risk of administering live viral vaccines to patients with immune suppression.
- 00:33:31 So why viral vaccines are specifically attenuated so that a normal, healthy homes can control that live viral vaccination an entity.
- 00:33:41 And essentially destroy it over time, such that were able to produce the response over a limited period of time that problem comes your immune suppressed.
- 00:33:51 ally viral vaccines can certainly get out of control, as you see here this particular picture will go into details about which vaccines are live virus what are really.
- 00:34:03 pose a risk for patients with them, yet suppression.
- 00:34:09 So Pearl for the day I gene the reactions of vaccines are almost always caused by additives or residual vaccine components, such as jelled it's not the active agent itself.
- 00:34:23 here's a list of some of the common vaccines and what some of those are some exceptions are that can really cause those reactions and we see there's a whole list that can be very.
- 00:34:36 What I would tell you it's also important to note that the components buried by manufacturer So yes, hepatitis B so nice and influence as they get gelatin, but not every influenza vaccine has a gel.
- 00:34:50 So, quite often individuals, even if they have a predisposing allergy to one of the components, there are alternatives for which they can receive the vaccine.
- 00:35:00 So an allergy component also does not necessarily mean you're going to be allergic to a vaccine so quite often we have patients who are identified in our specialties being allergic day.
- 00:35:11 They think and are under the impression that they're going to react every vaccine that contains.
- 00:35:18 So it's that art of assessing individual risk perhaps related to the severity of the area of our preexisting allergy, they may.

- 00:35:27impose how we approach those patients, whether we test them, whether we give them a great challenge and other things, but the take home lesson is there's usually a way to administer a vaccine to those individuals, despite a preexisting allergy to COMP.
- 00:35:44And then, finally, more importantly, and most importantly for everyone here, I hope you are aware that egg allergy really is no longer a concern for flu or.
- 00:35:55Certainly, a concern for patients, but from a care provider standpoint, there are very few precautions that need to be taken for administrate flu or Mr patients with a pre existing egg allergy.
- 00:36:08However, do not increase COMP content for yellow fever rabies vaccines, we still have a reason to pause and will sometimes do some extra things for those patients.
- 00:36:20So what about egg allergy and inactivated flu vaccines so 28 studies have been evaluated over 4000 patients have successfully received their vaccine, including 656 with severe allergy.
- 00:36:35Ariane eventful that mean no reactions at all, but very few significant reactions that caused any concern whatsoever, so there were some low rates a minor reactions that he can see, but really no greater rate but controls.
- 00:36:51So what this information tells us as that are precautions which we had been doing for years of doing pre vaccine skin testing and sometimes stepwise challenge was really unnecessary and a barrier to vaccination.
- 00:37:06So individuals that have an egg allergy are indeed able to receive inactivated influenza vaccination without additional measures.
- 00:37:17And for those who are leery every year for the last couple of years, there have been egg free products that are available for administration this past year was blue block and facilities.
- 00:37:31Alright, so which components caused an adverse reaction I gone over several in that last chart this one shows us a list of all of the common vaccines and some of the common components that we see.
- 00:37:45And I show here on the right hand side, the fact that all of those things that commonly cause.
- 00:37:52adverse effects and routine vaccines are not really contained in the code 19 so we have these calmer conversations with patients all the time.
- 00:38:01i'm allergic day I'm allergic to gel and I can't get the COVID 19 vaccine well it's important for everyone to note that none of it is in those two vaccines.
- 00:38:10What is in those vaccines are the active component and let them pick peg is not in any of these vaccines, but there is a related polly sorbet.
- 00:38:21Usually polly sorbet 20 or policy or maybe.
- 00:38:24The cross reactivity is putative it can be demonstrated of each row clinically and we haven't seen it we've been giving these vaccines and the routine schedule for years and I'm really not seen any reactions attributable to the poly sorbet component.
- 00:38:40So certainly reason to pause or consider, but the fact is that we have yet to see peg or poly sorbet as a definitive causing allergic reactions for either the routine pack seeds or the coconut 19 minutes.



- 00:38:58 And what about alpha certainly we learn more each and every year, so we've been testing for gelatin format and identified it as a risk factor for some of these common routines quite commonly.
- 00:39:12 Now, with the retrospective scope we might need to go back and read look at those individuals and see which ones were actually do TAO for Gala not the jello gelatin alone.
- 00:39:23 itself so here's a case published by cosby stone at vanderbilt a five year old that anaphylaxis after three different vaccines mmr varicella and detail by vv acquired vaccine.
- 00:39:37 Their approach was the skin tested gelatin and vaccines that contain gelatin, as you can see here and Mr varicella were positive, as well as the gelatin certainly appears like gelatin may have been the cause.
- 00:39:52 Well, they then went back and also checked specific ID and serum for alpha Gal and it was hugely positive.
- 00:39:59 So certainly alpha Gal can be a cause of concern for individuals receiving certain vaccines and this is a newer revelation for us as we approach our patients and.
- 00:40:11 We recommend these individuals undergoes specific counseling before receiving specific vaccines that contain non-human primates and Malian products such as mmr varicella and these common vaccines listed below.
- 00:40:28 Alright, so what did we do with our case or way back when we took a similar approach we did a prick and ID skin test and then challenged.
- 00:40:38 was our generic approach when we tested all for vaccines have that healthy for a month all experiencing a systemic reaction.
- 00:40:46 We noted, there was the negative both pricking ID skin test to have be detached and IP so we went ahead and Minister, the fall knows it did just fine we skin tested to the hip conjugate.
- 00:41:00 The skin test was negative on product, but was barely positive on it, we still had a low concern at this.
- 00:41:07 baby was a risk with the subsequent does but we're a little cautious and administered a great challenge, beginning with the 10th of the dose and sure enough that the patient experience hives leasing and a flare there is indicating a systemic allergic reaction.
- 00:41:25 So we were really wanted to know what was the cause of the reaction for this individual baby, if you will, in four months or six months of age at the time.
- 00:41:37 So I contact the manufacturer ask them to send me the vehicle to see for some exhibit in there, which is what our suspicion was that they're reacting to but.
- 00:41:46 I also asked for the conjugate purified protein itself, so the hip conjugate.
- 00:41:53 Is a poly saccharine conjugate vaccine and, in this case it's a CRM 197 protein now talk about just a minute derived from diphtheria.
- 00:42:03 And Sure enough, the vehicle was negative, but this specific conjugated compound it was positive.
- 00:42:09 So really wasn't due to the hip Kong which almost never isn't it wasn't due to the accepted in this case, there is the possibility of having conjugated specific our key.
- 00:42:21 And it has implications, with what this individual can be vaccinated with in the future, and there have been a couple of other cases published since then.
- 00:42:32 That has shown specific allergy to the conjugate portion of vaccines, so why use a conjugate to begin with one, it increases the advantage in this city of.

- 00:42:43 Really bland antigens trying to hope immune response like come off the lesson plans it has a single.
- 00:42:51 amino acid substitution that keeps it stable and it's really an automatically inactive and nontoxic, so it all looked good, and it does promote a great immune response.
- 00:43:01 By can be problematic for some individuals and this particular conjugate is still used in many vaccines it's no longer used to have the cause reaction in the baby.
- 00:43:12 But I understand some of the newer vaccines, including PC TV 20 just approved last year and then new a tumor vaccine uses it as a conjugate as well, so it's something for us to look out for.
- 00:43:28 Despite the scoop two cases most patients with preexisting allergy to vaccine components indeed tolerate that so that's nations without having to go through those brake lines of skin testing, it does challenges.
- 00:43:42 So a recent review and really published in in practice parameter format.
- 00:43:49 Are what to do with common presenting scenarios of patients with preexisting allergy, and it was based on a wealth of data accumulated over the last couple of decades showing.
- 00:44:00 That patients with immediate type allergy to minor components, such as milk Easter latex.
- 00:44:07 can receive these vaccines and our usual manner, without a lot of steps to go through to include skin testing the vaccine or greater challenges.
- 00:44:16 we've already talked about egg we can do all of those except for yellow fever.
- 00:44:21 And for individuals with gelatin they do recommend being a little more careful and part of that I think is the emerging alpha gals story, so we should look at patients have a gelatin analogy, a little earlier if we can't find.
- 00:44:34 alternatives for that particular type of vaccine so for dth or not I G mediated reactions.
- 00:44:43 If it's a minor contact allergy to something like an antibiotic or thumb aerosol the recommendation is indeed to administer all vaccines and unusual manner.
- 00:44:53 But I do recommend folks use their judgment and work with their patients to understand the level of anxiety, we are available to assist with those risk management, discussions and perhaps take some extra measures of do some testing Greta challenges when it makes the most sense.
- 00:45:13 Alright, so reasons to hesitate let's move on to what are the tree packages are vaccine contraindications and precautions, I think you might be surprised about how few there actually are.
- 00:45:27 So, which are these are contraindications the vaccination.
- 00:45:31 While acute illness can't get my vaccine because I'm sick today I'm on an antibiotic so I can't get my vaccine today i'm in the convalescent phase of an illness preterm birth is that a reason not to vaccinate recent infectious disease exposure.
- 00:45:49 And a history to penicillin or other drug allergy or non-vaccine allergy relatives with allergies or I'm on allergen immunotherapy a common thing comes up.
- 00:46:00 and frankly I've had an is history of qiangba race, I think you can all guess what the answer is none of these really serve as true package.



- 00:46:10insert constant contraindications there are a few considerations like have been for prematurity less than two kilograms and wellness negatives to certainly some exceptions to these roles, but by and large, these mild illnesses are contaminated that should rarely pose a barrier to vaccination.
- 00:46:34reaction does not equal contraindications so just a reiteration that wild vocal reactions a constitutional symptoms are often expected adverse events.
- 00:46:44That occur with normal vaccines, so they should not country indicate future dose and then rarely dth to a vaccine constituent can lead to local reactions that to should not prevent you from being vaccinated in the future.
- 00:47:01So, specifically, and I know this is a complex chart, but I think it's important to see all of the vaccines listed and to see the patterns that emerged with respect to true packages are cons contraindications and precautions, so it will begin with.
- 00:47:20The vaccine components and our, so it is important to see that there's moderate to severe illness that can occur, but it is listed as a precaution.
- 00:47:32Not a true contraindications an allergy to compound and it's certainly reason not to give a vaccine and but as we talked about it can be given a lot of instances such as.
- 00:47:47These and read our patterns of individuals who pose a special risk factor, those with compromised immune systems.
- 00:47:56There are several absolute contraindications of the as you might guess, they all deal with live attenuated vaccines that might get out of control lip administered to an immuno suppressed individually.
- 00:48:09So these are unbreakable ones, for the most part, except a very, very distinct circumstances and recommend or for all for evaluations of those that are contemplating giving the high viral vaccines to those with known to me suppression.
- 00:48:27So the other one that comes up quite often are individuals with Dr Murray Citroen so again going by just what's in the package insert gamma Ray less than six weeks prior to the dose is a prakash.
- 00:48:42that's it has nothing to do with who have which was what the cause of the gbs was or whether it was that specific baxi just having GPS within the last six weeks is the precaution.
- 00:48:55So, it stands to reason, if I had gbs following another reason why is elicited as a precaution, while it is a reason to hesitate, and certainly have to have those conversations, but it's important to know what the FDA and what the package insert.
- 00:49:10precautions and contraindications are three each of these vaccines, as we talk with our patients overture is again vaccine COP on its concern as contraindications.
- 00:49:24Other reasons to pause or consider pausing here, we see the CDC recommendations with respect to vaccines during pregnancy.
- 00:49:35There are few that are contraindications as you might guess that are alive viral variants.
- 00:49:42And smallpox is country indication, but in the setting of an exposure the benefits outweigh the risk.
- 00:49:50Those in green there are actually a few that are absolutely recommended during pregnancy pregnancy and i've listed those for you.

- 00:49:58 ones in blue or circumstance relevance, you have to weigh the risk of benefits but, again, there are very few that are contraindicated and really the only ones that are country indicated, or those that are live viral area.
- 00:50:15 Now they're precaution that we don't often think about his recent receipt of blood products or immunoglobulin containing products and this comes up mainly when we're trying to administer measles or varicella backs.
- 00:50:29 So you see here that there's a spread of recommended intervals between the time of blood product administration.
- 00:50:37 And the time of vaccination these little service ourselves, and you can also tell it there well beyond the typical half-life of three weeks for an ICT containing product, these are the top or poly immune essentially and human derived the recombinant ones pose very little risk, if not.
- 00:50:59 I will tell you there are also other trends that higher doses lead to longer, and so the longest interval is 11 months for him in a logical inventory doses of either either big or subcutaneous administered and.
- 00:51:13 So the immune suppression from this is a reason why you want to administer these as well as preexisting immunity that these vaccines that may limit or impair the uterus follow me response when it but it's true.
- 00:51:29 What about parenting antibiotic use is that a country vacation the vaccine.
- 00:51:35 While it depends oral typhoid, cholera for select antibiotics so essentially yes, if you're receiving a vaccine, that is against the active component of a live virus vaccine, you should hopefully have the opportunity to lay administration of the vaccines get the full effect.
- 00:51:58 Revisiting immune suppression.
- 00:52:01 Those receiving active cancer treatment immuno suppresses for transplant or stem cell transplant within two years on medications.
- 00:52:10 Primary mean deficiency followed in our clinic or elsewhere, advanced or untreated HIV infection and active treatment with high dose steroids or other suppressants.
- 00:52:22 they're not absolute contraindications to administering a vaccine, but we need to have those risk benefit discussions.
- 00:52:30 So the real risk is immune suppression, with the live viral vaccines is, it is a contract cation as we talked about.
- 00:52:38 But we also understand that the full immune response may be limited to the angels, who are immunosuppressed are receiving can come at me suppressive therapy.
- 00:52:50 doesn't mean you shouldn't do it, in fact, the benefits of even a partial response, while on immune suppressant or in an immune suppressed state.
- 00:52:59 Usually will outweigh the risk associated with vaccination or acquiring the disease something we've seen with covert 19 vaccines and the recent recommendation to for those who are immunosuppressed to get a fourth those.
- 00:53:14 So yes, you might not get a full reaction, but even some is better than not.
- 00:53:21 Where I think a lot of research needs to be done is really define those bullet points of where the risk of and insufficient being response occurs with respect and you know modulator and.
- 00:53:33 Administration and really where the risk is for these viral vaccines and other things when they're actually needed we don't know where those cut points are in the.

- 00:53:45 spectrum of patients on various levels of immune suppression having that information would help us better advise what to do with vaccines, right now, so it's oftentimes a guessing game.
- 00:53:58 So let's put these rare vaccine adverse events in context as well we focus a lot on anaphylaxis and it earlier.
- 00:54:06 Here is a case definition in our own practice parameters pretty classic for diagnosing handful acts as if you will, less than four hours more than one organ system.
- 00:54:17 And then, a possible anaphylaxis reaction, a single organ system or greater than Oregon system with a little bit beyond that four hour window that you would expect.
- 00:54:29 This comes up without for Gala as you might imagine the Brighton collaboration is also developed their own specific definition has been used in a lot of pivotal studies sudden onset rapid progression and at least two body systems, notably they drop out GI not quite sure why but.
- 00:54:49 This has been a relied upon definition of anaphylaxis and certainly use for the curve in 19 seasons.
- 00:54:57 Do you often recognize that anaphylaxis is pretty common not common and frequency but common across the spectrum of vaccines.
- 00:55:07 I like to try and remind folks that all vaccines have a risk for anaphylaxis, this is not a new phenomenon for 19.
- 00:55:16 So this publication shows that the relative risk or rate per million doses that have occurred with most of the common routine vaccine.
- 00:55:26 you'll see there rabies on the Left that does stand out, and the reason is that some of those older preparations had a much higher content of a Gal.
- 00:55:36 and lead to those anaphylaxis reactions for patients who were prescreened for egg allergy certainly that is decreased, with some of the newer preparations so let's put that in context.
- 00:55:50 Some of the newer vaccines that have emerged for coven 19 So if you combine all of these the relative risk for anaphylaxis for anti-vaccine is 1.31 particular.
- 00:56:01 publications recently about anaphylaxis occurring with the cove at 19 vaccines somewhere about 11 for a million for Pfizer and 2.5 million for Madonna where the estimated risk earlier.
- 00:56:16 Those figures, I think, are still high estimates and the signal is probably right where it should be at 1.31 for those vaccines.
- 00:56:26 But the current data has a little bit or multiple fold higher but still well within what we see for some of the other vaccines, on the work.
- 00:56:35 So, yes it's arrest, yes, it does occur, but it's really not out of the range of what we seen with other vaccines.
- 00:56:43 So quick shameless plug about our study here uva my side ti for a sponsored study we've just completed the adults and it pivoted to doing it children aged five to 11 year old looking for the occurrence of anaphylaxis or immediate type symptoms so.
- 00:57:02 I'm very excited to see the adult data, I think we will have.
- 00:57:06 Better prevalence data with them what we just saw on the last slide and, more importantly, start to identify some of the risk factors and some of the immunological changes that occur for some of those early reactors to vaccines.

- 00:57:22 So some of the less common events that we see with vaccines, including covert 19 vaccines are shown here highlighted my own car died is here.
- 00:57:32 reminding folks that the risk of some of these adverse reactions that occur in light for with natural infection usually exceed what we see.
- 00:57:43 With vaccination and that's certainly the case here with my own cordite is occurring, yes, but much less frequently than the setting of code 19.
- 00:57:52 disease itself, I highlighted them fad not that the on the left there under vaccine access risk So if you look on the chart here you'll see that that big blue spike I frankly think it's a matter of wonder reporting and setting of koba disease and found out that these much more common.
- 00:58:13 But it has created a lot of problems for individuals.
- 00:58:19 Who are undergoing imaging for certain reasons well beyond coven it vaccine or monitoring their disease.
- 00:58:28 So low fat and apathy is indeed comment and curves about 1% with the Mr na vaccines were from 0.321% I actually think it's a little higher.
- 00:58:39 clinical studies are the pivotal studies for getting era approval for these vaccines demonstrated 14% I had axillary swelling or tenderness.
- 00:58:50 And that does tend to decrease with a so the symptom onset is usually within the first couple of days, and it usually starts to subside after the 10th day.
- 00:59:01 But the real issue, as it can be a real confound are for folks undergoing imaging for other reasons, so here's a publication, the journal nuclear.
- 00:59:11 from last year 274 patients were undergoing pet CT for their malignancy surveillance or other reasons.
- 00:59:19 And they looked at individuals who underwent these studies within a month of vaccination.
- 00:59:25 And they you are able to demonstrate increase uptake at the site of vaccination the posterior our hand on the FCC lateral side of vaccination, where you see.
- 00:59:35 them fat not that the occurring from the draining lymph nodes of the side of vaccination and this particular study they looked at outcomes of lymph node uptake and what they dubbed as the double side appearance of bolt injection site and local, regional, of that.
- 00:59:55 So, if you look at the data lymph node on axillary on the left more common, knowing the purple bars after the second and after the first not too surprising.
- 01:00:05 Overall rates of 60%, so this is a very, very common fight on the right hand side that double sign of the uptake in two locations again common after the second one disappearing, a little bit quicker than the axillary lymphedema.
- 01:00:25 So this has been a confounding issue, particularly for those brilliant breast cancer cancer screening and mammography a.
- 01:00:35 subject matter scientific expert panel was confirmed, and these are their current recommendations for how to deal with this issue and not that these indiana frequent finding after vaccination.
- 01:00:48 that's a nation shouldn't be delayed do the upcoming energy because we now know that occurs and what to look for.
- 01:00:54 When there is the option, the recommendation is to schedule it before the first of a series of the vaccination, or at least six weeks after if you have some schedule flexibility.

- 01:01:05 And certainly advise your patients the risk of the occurrence of this little fat not, I think, so that they're not surprised.
- 01:01:15 So that does bring us to educating and informing our patients with facts, we have to remind them that.
- 01:01:24 Safety's at the first front and foremost of every step of the vaccine development administration cycle, whether it be the preclinical studies or the phase one studies really designed exclusively for safety.
- 01:01:38 Safety is still monitor throughout phase two phase three the FDA review certainly next week, when we need on the vaccines for kids it's going to be the biggest point that we look at.
- 01:01:50 The AC IP and CDC review this data religiously to come up with their recommended and custom group recommendations for specific vaccines and.
- 01:02:01 Postmarketing surveillance is really key to our identification of the less common adverse events so a quick plug for reporting to the vaccine adverse event reporting system.
- 01:02:15 It is incumbent upon us and really a mark of professionalism to report to there's even one it's uncertain whether the vaccine has caused the I do remind folks that anyone can report directly to there's even patients and they often.
- 01:02:34 So when that occurs, you can often get a confluence or really a whole lot of data that can be very difficult to decipher so I did take a snapshot of open pairs.
- 01:02:47 of what has been reported for covert 19 vaccines, as of a couple of weeks ago.
- 01:02:52 And it's critical for us to help distinguish what the true safety signals are from natural events and confounding conditions.
- 01:03:01 So there are a million reports on Cobra 19 vaccine adverse events includes over 25,000 per mile curtis.
- 01:03:09 And over 21,000 deaths following vaccinations, so I don't think there's anybody on the zoom thanks that.
- 01:03:17 coven 19 vaccines cause 21,000 deaths, but this is the type of data that gets into the late press and it's important to know that the background right it's almost never deleted from those assertions our courts.
- 01:03:36 This is the various reportable event table, and in fact the public health service act and mandates that we report these reactions when they occur.
- 01:03:46 The ones on the left are occurrences that occur after any vaccine and there are some specific vaccine related adverse events that there is particularly interested in and are bound to report once identified.
- 01:04:02 So that leaves the patient really in a dilemma.
- 01:04:06 And our challenge of understanding, where they are at with respect that they're hesitancy for vaccines, so the fear of consequences, the fear of disease consequences.
- 01:04:16 How do I make that risk benefit decision and that's where we come in to help give them the facts and evidence to help make a decision that's mutual and best in their best interest So what are, what is the best approach to vaccine has a patient so.
- 01:04:35 that's probably not the approach on always use for air old, I guess, a lottery works it's certainly not something I would do routinely.
- 01:04:43 But there are resources and suggestions as to exactly what to do to help approach vaccine hesitant patients, so the AMA is published.

- 01:04:55 Some recommendations and it'll build and show you here.
- 01:04:59 They want us to ask patients why to really counter misinformation with facts All this makes sense, know that we have to make a trust bond with patients, so that they can get to the right decision for them.
- 01:05:12 I highlighted this one don't be afraid to tell patients that need to get the vaccine, there have been several studies that it said, what is the number one reason you didn't get vaccinated and the answer was one of my physician never told me, I should.
- 01:05:27 So I implore you to have these types of conversations know adjust layout facts but also help them get to a decision.
- 01:05:36 That is right for them, sometimes we do need to provide our own recommendations and really tell them what our perspective is as to whether they should get vaccinated.
- 01:05:48 And certainly tailor the message, based on the patients that you have and meet them where they are with respect to their fears you're not alone.
- 01:05:57 There are several public resources to help I accumulate and stay aware of the facts of vaccine hypersensitivity those are listed on the left.
- 01:06:07 and Dr Ken Dr Smith and myself and the rest of the division or resource to you for anything with respect to vaccine adverse events, except being testing, we will test vaccines, when we have them on hand and we're certainly there to assist with your risk assessment and counseling.
- 01:06:28 Multiple areas of vaccine research are needed, from my perspective, I was very excited to sit in on the Medical School disparity conference a couple of days ago.
- 01:06:39 And one thing that wasn't discussed much was vaccine health, and I think there is a right area of research here uva really nationally in this area.
- 01:06:49 And as an immunologist the risk factors for either insufficient immune response, or the determination or development of adverse events is a great interest to me, so there is ongoing research and opportunity to look into that i'm excited to play a part of that here up.
- 01:07:09 and other features, such as the correlates indoor ability of immunity have really confounded as as we've looked at the.
- 01:07:17 Yes, we can show it reduces disease, how long that immunity last, what are the true measures that I can do a blood test and identify where you're at with respect to your protection or far away from it, we need to be able to get better.
- 01:07:35 So i'll leave you with a couple of numbers to think about 12 That was the number of routine vaccines on the CDC or AC idea don't schedule and I host more there on the pediatric scheduled.
- 01:07:51 29 vaccine preventable diseases that have ravaged the world in the past that we now have under control at risk.
- 01:08:01 Our individuals and communities who are straying away from these routine vaccines and we see the emergence of once control diseases such as measles 14 million routine scheduled vaccines that prevent disease.
- 01:08:19 220 million number of vaccines administered annually here in the US \$9.9 million reduction that direct health care costs each 33.4 million reduction in healthcare indirect costs each year here's the opportunity.

- 01:08:38 Still 2000 deaths per day of COVID-19. 22.7 million kids not vaccinated worldwide with something as simple as diphtheria, tetanus and pertussis up from 3 million not down up 3 million for three years ago.
- 01:08:56 74.3% US COVID-19 adults that are fully vaccinated it does have a couple of months ago.
- 01:09:04 And 45% of US COVID-19 have gotten their boosters there's a lot of opportunity with respect to vaccines out there.
- 01:09:12 And us having the greatest knowledge of the true evidence of both risk and benefit is going to help close some of these gaps.
- 01:09:22 So these are my parting shots for you keep the vaccine conversation front and center knowledge is indeed power, please educate your patients and each other.
- 01:09:33 never miss an opportunity to vaccinate prevent disease and we're here for you within the asthma allergy and methodology division, and again I thank you for the opportunity to present today, and look forward to answering your questions and see seeing you in the hallways very, very soon.
- 01:09:56 turn it back over to you for any questions.

#### **UVA IM Chiefs**

01:10:00 Thank you, Dr Nelson and for anyone that has questions you can either pop them into the chat or request to be unmuted and I'm happy to unmute you.

#### **Mike Nelson**

01:10:16 managed to stay on time that's great.

#### **UVA IM Chiefs**

01:10:38 looks like you've covered everything and it's super crystal clear, it was a fantastic presentation does anyone have any last minute burning questions, otherwise.

- 01:10:51 All right, oh, we have a question in here from Dr Dre Sir, do you anticipate will need yearly COVID-19 vaccines, or is it too soon to say.

#### **Mike Nelson**

01:11:03 Yes, I anticipate we're gonna need a regular schedule I don't know how frequently.

- 01:11:11 think I was a mistake to consider these as a single dose or to dose vaccine that was going to provide a it's a long duration of an entity.
- 01:11:20 I think read looking at how we administer that primary series may lead to longer duration installation of cellular memory and other mechanisms that will make that amenity last longer.



- 01:11:33 But in the short term, as we see various emerge and we uncover the fact that they are is waning, a mere de with time from some of these boosters.
- 01:11:43 Whether it's yearly every other year I don't know, but I do anticipate the need for frequent vaccinations, I look forward to the exciting research, including here at the university.
- 01:11:54 of universal vaccination against code in 19 at some of these disease.
- 01:11:59 So the magic bullet that gets that the virus itself that's really bulletproof against some of the variation we've seen in the receptor binding domain and other areas.
- 01:12:09 Are the types of vaccines that are going to be long lasting and they get us out of this requirement for having to do it all vaccinations.

### **UVA IM Chiefs**

01:12:19 Thank you, Dr Nelson Dr Logan wants to ask a question i'm going to unmute him.

- 01:12:25 yeah oh hi Dr beloved.

### **Rasheed A Balogun**

01:12:26 Thank you very much thank you, Dr Nelson my question is straightforward it's what your opinion is about how to deal with situations where.

- 01:12:39 Colleagues, people who are physicians themselves are contributing to the public discourse are contributing doubts in the community about the safety and efficacy of vaccines.

### **Mike Nelson**

01:13:00 yeah.

- 01:13:02 it's a great question that's The primary reason why our board American Board of algae immunology put out a misinformation statement we think it's a market professionalism.
- 01:13:14 To can be contributing to misinformation, the public that leads to putting patients lives at risk and not letting them receive the care that they should probably receive.
- 01:13:26 There are several approaches to it usually direct is the most appropriate one to pull those individuals aside and have healthy discussions about what you know, compared to what they know.
- 01:13:40 But there are also other reportable mechanisms to include the state medical board and their professional societies and their certification board.
- 01:13:49 They are all standing by to receive those requests and have mechanisms to deal with patients that are really on the fringe of the standard of care for vaccine help and spreading information.
- 01:14:01 is a very difficult scenario, and I am always surprised at how prevalent, it is no matter where you go there are going to be individuals.
- 01:14:11 who have opinions that are outside the norm, not always incorrect because we evoke change by being outside of the norm and challenging the norm.

- 01:14:22 But when patients are put at risk, with respect to some of those decisions and some of the information has been putting out, we do have an obligation to step.

### **UVA IM Chiefs**

01:14:34 Thank you, we have a whole list of questions so next Dr James platt smells has a question for you I'm going to unmute you Dr plot smells if you want to go ahead and talk.

### **Mike Nelson**

01:14:45 To James.

### **James Platts-Mills**

01:14:46 hey Mike thanks for your talk quick question, I guess, I wonder how much reacted university.

- 01:14:52 plays into vaccine hasn't see whether it's under appreciated people, just like I know i'm going to feel punk after getting this vaccine and I don't want to do it, and specifically for the Madonna vaccine when it was studied.
- 01:15:03 Initially I think for immunogenicity was 25 micrograms was 100 vs 250 and they settled with 100 because 25 wasn't immunogenicity but now there's a poster dose it's 50.
- 01:15:15 Has you know, is the reactor Jeunesse the profile much better and did FDA I don't know was there, an opportunity that was missed to lower the approved dose to improve the profile we don't have many vaccines that are that reactive genetic that are approved.

### **Mike Nelson**

01:15:31 Correct I knew it was it's exactly as you laid out they've had the demonstration and the response and protective effect in clinical trials of their 40,000 patients.

- 01:15:43 I do think that you could achieve an equivalent level of protection at a lower dose however they didn't have the real world data and demonstration that.
- 01:15:53 There is reduced disease prevalence of launch vaccinated individuals at belts lower dose and the pressures of time and getting this to the market and hitting the pandemic head on, I think gotten away.
- 01:16:05 So I do think that you could get away with a lower dose, that is why they unlike Pfizer want what they have dose for their booster because they knew that.
- 01:16:16 After having been primed by initial vaccination primary series and or disease, they wouldn't require as much does.
- 01:16:25 So we may, there are a couple of vaccines on the market beyond Madonna or on the routine schedule, where the dose is indeed the booster doses and deep different than the primary does.

- 01:16:37And this may be one of those vaccines, where it will have to fit that category, but yes, there are opportunities to revisit not only the.
- 01:16:45Initial treatment does for primary series but exactly the intervals between doses, and what does primary series looks like I think is areas of research that we're going to see.
- 01:16:58I'll tell you James the biggest frustration with me is that these clinical trials have been rolled out and continue to be rolled out without paying all a lot of attention to preexisting immunity.
- 01:17:11So individuals have gotten infected previously how they respond to vaccines are being lumped in with those that are essentially disease so.
- 01:17:22it's difficult to sort out with all of that mixed population what the true schedule should be and what the true dosing Regiment should be your point is well taken.

### **UVA IM Chiefs**

01:17:34and kill and then we have Dr Tyson bell I'm going to unmute you.

- 01:17:40And who wants ask you a question as well.

### **Taison Bell**

01:17:43Nelson had a question about vaccine trials in pregnant women, because I think that's been one of the vexing things about the pandemic.

- 01:17:55Is that clinical trials initially did not include pregnant women that's their concerns there, but you know, hopefully we don't have to do this again anytime soon, but is there a way that we could.
- 01:18:06Try to enroll those who are pregnant and clinical trial to try to get in there more vaccine confidence.

### **Mike Nelson**

01:18:15Yes, Sir, there is desire and certainly thirst for primary inclusion and initial trials.

- 01:18:23I don't really see it happening at the forefront, to be perfectly honest, I think demonstration reactive generosity.
- 01:18:30and ethics is going to be done in the normal, healthy population and the pregnant population is going to wait, just like it did for this coven 19 vaccine.
- 01:18:40Their approval process relies on demonstration of bridge immuno bridging and safety data for different populations, so the reason we're getting down to the younger age group is demonstration and a healthy population that's most common.
- 01:18:59believe that the risk associated with vaccination during pregnancy are still going to be a barrier way to.
- 01:19:07Do clued in the front end of vaccines that are initially rolled out I wish it were the case.

- 01:19:14 And I think that was one of the primary reasons why emergency use authorization mechanism was chosen for getting it to the market.
- 01:19:24 One they hadn't had the longer duration of follow up that's typically required for full approval of a backseat, but they also understood that there were other populations who were not in the original.
- 01:19:37 trial that needed and deserve that vaccine and that experience and data could be achieved by administering those vaccines and that's exactly what happened so within the first couple of months.
- 01:19:49 Patients who were pregnant were receiving the vaccines, as they always do, and we identify them through right registries and other things we look at their outcomes and we're able to accumulate that knowledge over time.
- 01:20:03 So I wish I would say yes we'll do dedicated pregnancy vaccines out front and less the risk is clearly there that I just don't see it happen be perfectly.
- 01:20:16 Great question.

### **UVA IM Chiefs**

01:20:18 We have three more questions so from Dr Alden Doyle and wants to know about your thoughts on fourth doses for transplant patients or fifth doses for non-responders.

### **Mike Nelson**

01:20:32 So for transplant and really immune suppressed I thoroughly in favor of boosting the immune response in our lab we've been able to track the climate, at least he roll immunity over time, it is a real phenomenon, it does not appear to be going away after the third dose.

- 01:20:52 From data from other labs and certainly those at the highest risk of disease are immunosuppressed patient so maintaining a high-level banner body well indeed prevent some of those severe outcomes, with respect to disease infection.
- 01:21:08 So the so called breakthrough infections, the vaccines were never designed to prevent infection totally they really weren't prevent.
- 01:21:16 designed to prevent severe consequences of disease, but they can be very devastating and are immunocompromised population.
- 01:21:25 So anybody on high doses of immune suppressants as well as those with underlying conditions, including transplant.
- 01:21:33 should look to take advantage of those booster doses when they're recommended available So yes, five months after the last dose I would recommend that our transplant patients receive them.
- 01:21:45 With the understanding that they may not achieve a for response, but this is one of the scenarios, where a partial responses beneficial.

### **UVA IM Chiefs**

01:21:55 Right Thank you um and then second to last question from Dr Bergen did you have any thoughts about Aaron Rodgers and being allergic to components of the vaccine.

### **Mike Nelson**

01:22:07 i'm not going to comment specifically on individuals but yes, there are that's one of the reasons I chose this talk.

- 01:22:16 To be perfectly honest, I wanted to dispel some of them that's that allergy to account owner vaccine doesn't necessarily mean that you shouldn't get the vaccine.
- 01:22:27 And I think I showed you throughout the entire talk that there are individuals who can receive vaccines, despite an allergy to the component themselves, so I would implore that individuals.
- 01:22:42 get the best information seek out their care provider seek out a specialist to have those true risk benefit.
- 01:22:49 Does discussions and do the necessary testing and challenges when it's appropriate to really state that that's the case.
- 01:22:58 There are certainly risk for individuals propagating this that an allergy to a specific component or an allergy in general means that's a reason that I shouldn't be vaccinated that's why we're here today to learn more so that we can educate our patients.

### **UVA IM Chiefs**

01:23:14 And our last question we have what to say to clients with history of P amp D vt who are still concerned about blood clot issues that were previously occurred with vaccine administration.

### **Mike Nelson**

01:23:30 may have included a slide in here for.

- 01:23:39 So here's the code 19 vaccines and some of the rare side effects of the top is a j&j vaccine the bottom, the 2am in our back Mr RNA vaccines.
- 01:23:50 So gamma Ray syndrome and the risk is essentially higher in males and females in the older age groups, but this traumatic risk is really associated with the younger female age for the FDA advisory committee had.
- 01:24:09 great difficulty and expanding recommendations on what age group to administer booster Dallas's with this particular risk emerged after initial bets and.
- 01:24:21 So, having a history of DDT alone or an issue of hyper quiet gullibility.
- 01:24:28 Yes, can be a risk for some certain vaccines now, since we are not using the J and J vaccine much anymore, the recommendation would be to use an mmr vaccine with respect to convert 19 where the risk is much less.

- 01:24:43The risk is my new for having a hyper coil moment that, with all of these vaccines so for those individuals with a benign history of DVD even if on blood thinners for it, I would still recommend vaccination.

**UVA IM Chiefs**

01:24:59Thank you so much, Dr Nelson and Thank you everyone for tuning in.

**Mike Nelson**

01:25:08Thank you.