

WEBVTT

NOTE duration:"00:33:29.2630000"

NOTE language:en-us

NOTE Confidence: 0.937380969524384

00:00:05.140 --> 00:00:27.430 Welcome to a series of podcasts brought you by Yale University. This is doctor. Janine Evans associate professor at Yale School of Madison speaking on Lyme disease and the development of a vaccine in the mid 1990s as part of the Yale Peabody Museum's biodiversity and global change day and sponsored by a science Education Partnership Award from the National Institutes of Health.

NOTE Confidence: 0.932431519031525

00:00:28.260 --> 00:00:47.050 Thanks for inviting me the Lyme vaccine story is actually a very interesting one and one of the great things about it was the first description of Lyme arthritis happened in 1975, when some mothers in around the lime area.

NOTE Confidence: 0.962382853031158

00:00:47.570 --> 00:00:52.900 Notice that there was a high incidence of children who were diagnosed with juvenile rheumatoid arthritis.

NOTE Confidence: 0.950015127658844

00:00:53.600 --> 00:00:55.340 And we know that.

NOTE Confidence: 0.929481446743011

00:00:56.520 --> 00:01:20.760 That was way higher than what would have been expected for that patient population so they came down to Yale and engaged Steven Mellowest, a an Allen steer into investigating. It further so it was first described in 1975, an by 1998. We actually had a vaccine that was developed.

NOTE Confidence: 0.93137139081955

00:01:21.510 --> 00:01:51.520 Tried shown to be efficient and put out on the market. So it was a relatively when you think about it short span from start to finish with respect to Lyme disease. I think when you're designing clinical trials. One of the things that are important is what questions do you ask? What is it an important thing to invest time and energy into and what are some of the pitfalls that you can expect and what data do you need to gather?

NOTE Confidence: 0.939657688140869

00:01:51.520 --> 00:02:09.290 So before I get into the exact line vaccine trials. I want to give a little bit of background about some of the Epidemiology and ecology of Lyme disease because they have their very pertinent into what went on in the thinking about the Lyme Vaccine Development.

NOTE Confidence: 0.955105662345886

00:02:10.860 --> 00:02:23.050 So, in the means is a means of background. Lyme disease is really the most common vector borne illness that is reported in the United States and probably accounts for about 90%.

NOTE Confidence: 0.950069487094879

00:02:24.220 --> 00:02:27.920 Or 95% of all reported vector borne illnesses.

NOTE Confidence: 0.948665857315063

00:02:28.480 --> 00:02:43.170 In addition to that it has a very distinct geographic localization within the United States and in areas that are highly endemic up to 1 to 3% of individuals will contract infection from Lyme disease.

NOTE Confidence: 0.875054061412811

00:02:44.630 --> 00:02:51.250 Vector borne means that it's transmitted by.

NOTE Confidence: 0.901165783405304

00:02:51.810 --> 00:03:05.170 A tick or a mosquito or something else that bites. The individual flea all of those sorts of things that then deposit the illness and that's how individuals get it.

NOTE Confidence: 0.929828345775604

00:03:06.960 --> 00:03:39.190 So here are the 3 major areas where people developed Lyme disease. Probably the highest incidents is along the Eastern Seaboard. From about Massachusetts to Maryland. There's another pocket in Wisconsin and then a very, very small pocket out in California and again. The reason why the pocket in California is as small as it is, is because how the tick lifestyle actually is dependent upon feeding on lizards.

NOTE Confidence: 0.927846670150757

00:03:39.270 --> 00:04:11.180 And lizards don't propagate the disease as opposed to Wisconsin and the East Coast, where probably the biggest animal that is responsible for the perpetuation of Lyme disease is a Brown is the white footed mouse and they carry the Spira Kate with them. Even though they don't themselves get ill. But we also know that Lyme disease occurs worldwide typically in temperate areas, so we've got our pockets, in the United States.

NOTE Confidence: 0.93558669090271

00:04:11.180 --> 00:04:18.690 And then there's also abroad pocket that spans sort of the central part of Europe, all the way to Asia.

NOTE Confidence: 0.92882627248764

00:04:19.470 --> 00:04:51.600 And here's the the ones on the top which is zodia scapularis or the deer. Tick is what's responsible for transmitting Lyme disease underneath that is what's referred to as the Lone Star State tick, which is more

common in sort of Texas and southern parts of the United States and then underneath that is the dog tick and these are the various different stages of a ticks life. The eggs odious scapularis ticket has a 2 year lifespan.

NOTE Confidence: 0.900576591491699

00:04:51.660 --> 00:05:03.610 So the first, the first stage is the larval stage, so their hatched, they develop Marvi and the larva feed on animals typically small animals.

NOTE Confidence: 0.921022653579712

00:05:04.220 --> 00:05:23.990 Including the white footed mouse and that's how one that's one stage that the contract, the infection. The next is that they'll after they fed and drop off. They molt or grow up into being a nymphal stage and these are some of the most aggressive.

NOTE Confidence: 0.934912204742432

00:05:24.490 --> 00:05:54.400 Feeders in the ticks lifestyle and these are what the ones who were responsible for transmitting the most cases of Lyme disease because their indiscriminate about who they feed on humans dogs mice? What have you and then they drop off and then the following year. The adults emerge and their preference actually is to feed on deer and they are much, much less likely to transmit Lyme disease than than in full stages are.

NOTE Confidence: 0.87289297580719

00:05:55.200 --> 00:06:12.070 So the principle vectors of eggs odious scapularis, which is detect in the northeast in the Midwest is the IG Zodia Scapula Harris and it's a slightly different tick in the West coast and again their preferences to feed on lizards.

NOTE Confidence: 0.924305260181427

00:06:13.180 --> 00:06:17.630 Although you see this kind of tick in the S for.

NOTE Confidence: 0.938454031944275

00:06:18.150 --> 00:06:24.140 A number of reasons, Lyme disease is not as endemic there as it is in the N.

NOTE Confidence: 0.941000163555145

00:06:26.040 --> 00:06:39.820 And this is the bacteria, which is called a borrelia. That's responsible for causing Lyme disease. So this is what is the infection and it's these little squiggly bacteria?

NOTE Confidence: 0.869472324848175

00:06:40.320 --> 00:06:43.640 That are from a family that's termed borrelia.

NOTE Confidence: 0.951998293399811

00:06:46.060 --> 00:07:01.250 And we know that based on looking at the types of proteins that are present on these bacteria that there's actually 11 different kinds of Borrelia that have been described to date.

NOTE Confidence: 0.937190532684326

00:07:01.790 --> 00:07:20.020 And they've been given various different names, depending on who found them or where they were found, but only three of them to date has been felt to be associated with actually human disease and that includes borrelia sense of strict do.

NOTE Confidence: 0.660333752632141

00:07:20.540 --> 00:07:24.680 Paralia grinnny I am brelje absolved and sell side.

NOTE Confidence: 0.922253668308258

00:07:27.030 --> 00:07:43.850 So all of the Lyme disease borrelia that occur in the United States. All are from the census trick. Do class in Europe. You can get all three kinds, but Granny I, an observe see. I actually don't.

NOTE Confidence: 0.96244353055954

00:07:44.450 --> 00:07:46.370 Are present in the United States?

NOTE Confidence: 0.935506701469421

00:07:46.920 --> 00:08:00.200 And the difference between these various different species is that they expressed different proteins on their outside coats and so that can distinct one from another kind.

NOTE Confidence: 0.941752731800079

00:08:02.380 --> 00:08:27.550 And so if you mashed up those borrelia and you ran them out, so that they made different bands depending upon what their weight and size were then you'd get a picture like we see over here, so you see that there's lots. And lots of different proteins that are present on the Borrelia. Some of which the immune system responds to very, very aggressively.

NOTE Confidence: 0.758540272712708

00:08:30.480 --> 00:08:31.060 And.

NOTE Confidence: 0.904699504375458

00:08:31.850 --> 00:09:04.340 Some of the ones that seemed to elicit a very strong immune response are what's termed aspa, which is a protein on the outside outer surface protein a a being that it was described 1st and then B&C and they go DEFG and so forth, then there's one that's called a 41 kilodalton flagellin protein. That's not only its seeing not only in Lyme disease or umbrella.

NOTE Confidence: 0.946238398551941

00:09:04.340 --> 00:09:28.120 But also on lots of other different organisms as well, and then a variety of other ones that have been described and what the

researchers did when they found that there's these various different proteins as they actually were capable of being able to isolate them and then clone them so that they could grow up big batches of these various different proteins.

NOTE Confidence: 0.927911937236786

00:09:29.990 --> 00:10:00.040 And what they found was that even within OS pay. There are some variations that take place so that not all aspies are exactly the same OS pay. There's a little bit less of that kind of diversity, then what happens in some of the other proteins such as ASP see where there's lots more of that going on and again. If you're going to use one of these as a vaccine that concern would be if there's lots of diversity.

NOTE Confidence: 0.945491850376129

00:10:00.080 --> 00:10:04.930 You may not be able to be as protective does that make sense.

NOTE Confidence: 0.621245622634888

00:10:06.020 --> 00:10:06.540 OK.

NOTE Confidence: 0.951500058174133

00:10:07.430 --> 00:10:30.090 So the other question is, we've got Lyme disease and it can cause all kinds of problems. As far as illnesses are concerned. Thankfully, the majority of cases of Lyme disease are caught very, very early in the course of the illness and that's the stage of the skin rash and that skin rashes called erythema migrans.

NOTE Confidence: 0.93358838558197

00:10:31.690 --> 00:10:40.590 Other things that can happen and what are things like arthritis that tend to happen months after contracting the illness.

NOTE Confidence: 0.927889585494995

00:10:41.270 --> 00:10:52.880 You can get a facial palsy, which is a drooping of the side of the face certain neurologic things and sometimes it can affect the heart as well.

NOTE Confidence: 0.943298876285553

00:10:53.840 --> 00:11:08.580 Those are much more concerning and the longer that somebody's had an illness the harder. It is to try and get rid of it and sometimes people are left with symptoms following treatment.

NOTE Confidence: 0.941836476325989

00:11:11.010 --> 00:11:38.840 It would be nice to be able to prevent getting the disease in the 1st place. So 1 question is how do we go about protecting ourselves from getting Lyme disease so one thing is to know if the area that you're in has a high rate of Lyme disease, meaning that the ticks in that area carry a lot of disease or the percentage of ticks that carry the disease is high.

NOTE Confidence: 0.9224813580513

00:11:39.510 --> 00:11:47.170 We also know that takes like to hang out and would it in grassy areas. We also know that.

NOTE Confidence: 0.911146700382233

00:11:49.320 --> 00:12:00.360 Although they can occur on lawns usually, it's right on the edge of the lawn in conjunction or right next door bordering on sort of a hoodie, Woody area.

NOTE Confidence: 0.960671782493591

00:12:00.900 --> 00:12:09.930 And we also know that probably the people who are the most at risk for contracting Lyme disease are young children. 'cause they are out and about.

NOTE Confidence: 0.941291153430939

00:12:10.430 --> 00:12:28.630 And the interesting thing is the next and then there's this drop during the teenage in 20 years I guess. Maybe we're not out, doing things in the Woods as much. When were in our teens and 20s and then back up again when in the 30s and 40s, when I guess again people take on these recreational activities.

NOTE Confidence: 0.951659381389618

00:12:30.870 --> 00:13:02.880 So as far as prevention measures are concerned there's a couple of different strategies that people use or have been proposed in order to reduce the incidence of Lyme disease. One would be just don't go there and avoid any areas that have high rates of Lyme disease, which is kind of a bummer because a lot of them are along Cape Cod and Martha's Vineyard and places, that people like to go in vacation. We can try an reduce tick populations as best we can with insecticides.

NOTE Confidence: 0.922891974449158

00:13:03.070 --> 00:13:08.190 And one strategy and very high endemic areas is actually in the early spring when the.

NOTE Confidence: 0.76939469575882

00:13:08.730 --> 00:13:13.010 Than Imps are out to actually then do.

NOTE Confidence: 0.927438914775848

00:13:13.660 --> 00:13:18.060 Do a round of insecticide to try and reduce those populations.

NOTE Confidence: 0.939369559288025

00:13:19.360 --> 00:13:28.250 Another strategy would be to just try and get the deer out because we know they're important to sustain the adults that then.

NOTE Confidence: 0.915998220443726

00:13:29.010 --> 00:13:41.760 You know give rise to the Larva and etc. But to do that. You really would be very hard because you need very, very high fences and it just.

NOTE Confidence: 0.882435739040375

00:13:42.520 --> 00:13:43.270 Would be?

NOTE Confidence: 0.93959242105484

00:13:43.810 --> 00:13:56.970 Very costly in order to do that, you can protect yourself and we'll get into that in a second you can use repellents for ticks and lastly the issue about vaccination, which we're talking about today.

NOTE Confidence: 0.935150742530823

00:13:58.860 --> 00:14:22.090 So here are what's recommended as far as some of the personal protection. Things so make sure that you stay away from going out into the grass and the wilderness stay on the path. They suggest that you wear long sleeve shirts long pants. Tuck your socks in your pants into your socks.

NOTE Confidence: 0.919211864471436

00:14:22.690 --> 00:14:50.550 Wear light colored clothing, so that you can identify ticks. Easily wear a hat so that they can't get into your hair use repellent, an wear sturdy shoes now you and I both know that in the middle of July. This is a very hard thing to do so, although it's effective. It's not very convenient and people don't like to do it.

NOTE Confidence: 0.945327341556549

00:14:52.250 --> 00:15:10.550 We also know that if people pull ticks off what do you do about that if you found that it actually is a deer tick that you've pulled off they've done a number of studies looking to see whether or not a short course of antibiotics would reduce the risk of developing Lyme disease.

NOTE Confidence: 0.944400072097778

00:15:11.640 --> 00:15:24.950 And we know that even in highly endemic areas. If you pull that tick off within a 24 to 36 hour period your risk of contracting Lyme disease is extremely small so.

NOTE Confidence: 0.941215753555298

00:15:25.450 --> 00:15:49.310 3 very large studies really didn't show that the that the risk of having a reaction to the antibiotics outweighed. The fact that you reduce the development of Lyme disease. There was one study that showed if you gave a single course of doxycycline, which is an antibiotic that that actually did a little bit better than doing nothing at all.

NOTE Confidence: 0.929653644561768

00:15:49.880 --> 00:15:57.380 And at this point if you pull a tick off actually getting a blood test to look to see if you have Lyme disease is.

NOTE Confidence: 0.917919158935547

00:15:58.110 --> 00:16:01.580 Is typically negative test? It's not going to help.

NOTE Confidence: 0.459587454795837

00:16:03.080 --> 00:16:03.930 So.

NOTE Confidence: 0.940626919269562

00:16:04.520 --> 00:16:35.850 Is there a need for a vaccine? This is going to require a lot of resources a lot of money into the development. The marketing taking it from you know the observation of whether or not you found something that effective all the way to the point where at the FDA approves it and it's out on the market and this was very controversial through the whole course of the development of the Lyme Vaccine. The people will, who are in favor of it argued that Lyme disease is a major health burden.

NOTE Confidence: 0.93169242143631

00:16:35.850 --> 00:16:49.010 That there's lots of Los work that there's lots of tourist that particularly in endemic areas and estimated that the cost for each case of Lyme disease was about \$10,000.

NOTE Confidence: 0.908626317977905

00:16:49.700 --> 00:16:57.780 That, they also argued that the areas that were endemic for Lyme disease we're expanding.

NOTE Confidence: 0.923169314861298

00:16:58.700 --> 00:17:02.570 That some of the late manifestations can be very disabling.

NOTE Confidence: 0.924533426761627

00:17:03.400 --> 00:17:14.080 And that our other means of being able to prevent Lyme disease are not very their inadequate or people just aren't going to do them.

NOTE Confidence: 0.936438620090485

00:17:14.860 --> 00:17:22.370 People who argued against going forward with the Lyme Vaccine said that most cases are diagnosed early.

NOTE Confidence: 0.918837606906891

00:17:23.030 --> 00:17:29.980 When they're diagnosed and treated early people do extraordinarily well so why do we have to do this?

NOTE Confidence: 0.861708223819733

00:17:30.480 --> 00:17:36.130 And that it's it's rarely, if ever fatal.

NOTE Confidence: 0.914560317993164

00:17:36.860 --> 00:17:37.990 So it's not a killer.

NOTE Confidence: 0.929887592792511

00:17:38.670 --> 00:17:49.540 And that there was lots of concerns that potential side effects from the Lyme vaccine would outweigh any benefits that were found.

NOTE Confidence: 0.939265787601471

00:17:50.970 --> 00:18:14.230 But nonetheless it was moved forward and one of the first things that you try and do is find an animal model that mimics the disease that it is that you're trying to deal with, and so there have been a number of different animals that have that have certain features of human Lyme disease, but not all of them.

NOTE Confidence: 0.930944204330444

00:18:14.740 --> 00:18:47.070 And the one that probably most of the work has been done on have been mice because you know what the genetic background is you know it's easy to be able to measure some of the immunological things and so, if you give certain genetic mice. Lyme disease they will develop and arthritis and the paw on the left hand side is swollen and that's an example of Lyme arthritis and the other thing that they get is actually.

NOTE Confidence: 0.937538385391235

00:18:47.070 --> 00:19:09.840 Heart involvement as well so here we have a mechanism of looking to see whether or not. We can come up with a vaccine to prevent prevent mice from developing Lyme disease and we've got good ways of being able to see whether or not. They've gotten it an again measurement in their blood and from tissue samples.

NOTE Confidence: 0.929849326610565

00:19:11.310 --> 00:19:27.570 So they actually went they purified this outer surface protein a which is one of the proteins on the on the bacteria and they gave it to mice and then they look to see whether or not there was any evidence of Lyme disease.

NOTE Confidence: 0.941262245178223

00:19:28.840 --> 00:19:53.570 And they compared that with what's called the control population where they didn't give them the OS. Pei vaccine and lo and behold, all of the mice who were given the vaccine. None of them developed. Lyme disease as opposed to 100% of their controls were not given the vaccine every single one of them developed Lyme disease.

NOTE Confidence: 0.757987558841705

00:19:54.170 --> 00:19:54.770 And.

NOTE Confidence: 0.950656473636627

00:19:55.510 --> 00:20:02.370 The interesting thing that they observed as well is that if you gave you had to give the vaccine.

NOTE Confidence: 0.934587955474854

00:20:03.410 --> 00:20:19.640 Prior to giving an infection in order to have it be protective if you gave it afterwards. It was absolutely no good. And so it raised the question as to how is this vaccine working in the 1st place?

NOTE Confidence: 0.77848869562149

00:20:20.330 --> 00:20:21.000 And.

NOTE Confidence: 0.915840268135071

00:20:21.560 --> 00:20:26.970 The way vaccines typically work is that you give somebody.

NOTE Confidence: 0.931841969490051

00:20:27.730 --> 00:20:42.300 A protein or whatever against what it is that you're trying to fight and their immune systems develops a defense against it and then they go around doing sort of surveillance and if it comes across that then.

NOTE Confidence: 0.922108769416809

00:20:43.070 --> 00:20:46.720 Tries to get rid of whatever it is the offending Organism is.

NOTE Confidence: 0.924760401248932

00:20:48.310 --> 00:21:00.550 What happens in Lyme disease is that when you give them aspac? How it works? Is it actually as the tickets drinking in the blood containing those antibodies.

NOTE Confidence: 0.836397051811218

00:21:01.340 --> 00:21:11.680 The aspac antibodies wipe out the Borrelia in the stomach of the Tech.

NOTE Confidence: 0.916435599327087

00:21:12.640 --> 00:21:21.180 If you give it afterwards and they've already gotten infected that aspac antibody isn't affective anymore.

NOTE Confidence: 0.929030478000641

00:21:22.570 --> 00:21:27.090 And that mechanism is important to certain issues that came up later.

NOTE Confidence: 0.893700122833252

00:21:29.540 --> 00:21:36.620 So again how this is working is it's wiping it out in the stomach of the tick rather than.

NOTE Confidence: 0.942005932331085

00:21:37.230 --> 00:21:55.580 And so it would be important that you would have very high levels of this around in your body all the time and we also found that there was a certain portion of that. OSP a protein that was responsible for the protection that we saw in the vaccine trials.

NOTE Confidence: 0.929278671741486

00:21:56.120 --> 00:22:15.570 And the reason why it isn't effective after the fact is the fact that what that bacteria does is it is. It makes certain proteins. During various different phases of where it is at the time so when it synthetix stomach it has it.

NOTE Confidence: 0.893196940422058

00:22:16.090 --> 00:22:25.510 It puts on high levels of this OS. Pei protein the minute that it that it starts to feed and blood comes into the stomach.

NOTE Confidence: 0.840975403785706

00:22:26.270 --> 00:22:32.110 It takes the OS pay off an it ramps up another protein called OSP C.

NOTE Confidence: 0.937129855155945

00:22:32.940 --> 00:22:43.820 So the reason why it's not effective after the fact is that OS pay is no longer being expressed by the bacteria when it's in the human body?

NOTE Confidence: 0.927605271339417

00:22:44.730 --> 00:23:14.250 That makes sense so then we found that it was affective in mice. We found that if you gave it ahead of time that you could protect we found out how it actually worked and then it was time to take it on and see whether or not. It was affective in humans and when you do clinical research, particularly in vaccine trials and many other medications against illnesses as you do it in phases and your very first phase is.

NOTE Confidence: 0.929094791412354

00:23:14.910 --> 00:23:39.480 Is it safe to people tolerate it and what's the appropriate and then Phase 2 is? What's the appropriate dose that you need so the Phase 1 trial, actually took a number of individuals and gave them a spee and just to measure whether or not they their immune system responded to the vaccination and sure enough, at certain levels, it did.

NOTE Confidence: 0.919870555400848

00:23:40.350 --> 00:23:56.710 Then they asked whether what was the optimum dose so they did. Another trial where they did 3 separate dosing amounts and then found out that there was a certain dose 30 micrograms that really gave the best result.

NOTE Confidence: 0.939171254634857

00:23:57.680 --> 00:24:08.120 And then they asked the question well if you've already have Lyme disease and we're giving you this vaccination is it safe in those people and sure enough.

NOTE Confidence: 0.930155456066132

00:24:08.630 --> 00:24:19.470 It was people who had prior history of Lyme disease. It didn't matter. You didn't have a worse reaction. You didn't have a problem with it, and you were able to Mount a response.

NOTE Confidence: 0.917768716812134

00:24:20.850 --> 00:24:43.390 So having done that background work. It was then time to do. The real big massive trials and here there were 2 companies who actually developed a Lyme vaccine and that included Smith Kline Beecham and pasture merrier cannot and both of these companies did major trials and.

NOTE Confidence: 0.922780156135559

00:24:43.950 --> 00:24:57.590 And solicited 10,000 that's a typo. 10,000 people who are volunteers and they either got the 3:00 doses of the vaccine or they got placebo, which was nothing.

NOTE Confidence: 0.919200301170349

00:24:58.160 --> 00:25:09.670 And they gave it to them on a dosing schedule that they had also worked out under previous trials, which was your first dose. Then you got the second dose a month later and then you got the 3rd dose.

NOTE Confidence: 0.950812160968781

00:25:10.840 --> 00:25:12.180 12 months later.

NOTE Confidence: 0.941610157489777

00:25:12.940 --> 00:25:31.100 All the volunteers were given Diaries so that they could capture any kind of side effect that might possibly be experienced and they wanted to know everything again wanting to know whether or not. It was safe and whether or not there were there would be other issues related to the vaccine.

NOTE Confidence: 0.937793433666229

00:25:33.130 --> 00:25:58.590 And then they had to come up with what they decided to be criteria on what made up definite. Lyme disease possible Lyme disease. They also measured to see whether or not somebody could have been infected, but didn't know it, which is called asymptomatic seroconversion and they also did history, physical exams cultures polymerise chain reaction, which is a way of amplifying DNA.

NOTE Confidence: 0.923998475074768

00:25:59.190 --> 00:26:05.370 And they did blood tests looking to see if there was exposure to Lyme disease.

NOTE Confidence: 0.933302521705627

00:26:06.890 --> 00:26:37.530 And what they found was after the first two injections that it was protective about 50% of the time for definite cases and that it protected about 83% of the time from the asymptomatic seroconversion meaning that you've been exposed but you never develop symptoms. But after the 3rd injection that went up to 76% protective about definite cases.

NOTE Confidence: 0.881790995597839

00:26:37.700 --> 00:26:44.130 And 100% protective about from a symptom asymptomatic seroconversion.

NOTE Confidence: 0.936028718948364

00:26:45.010 --> 00:26:47.220 At this point we did not do boosters.

NOTE Confidence: 0.934582650661469

00:26:47.760 --> 00:27:16.350 And similarly I think although it looks a little bit better here. The pasture product. Gay very similar results. These side effect profile. That was associated with the vaccine were common. Typically they were short lived and were pain at the injection site. Sometimes some redness and some soreness similar to when you get a tetanus shot sometimes people develops a low grade fevers fatigue for a couple of days headaches.

NOTE Confidence: 0.933594286441803

00:27:16.880 --> 00:27:47.760 Joint aches and pains, but again, these were usually lasting maybe 1 to 3 days and there was no difference between any serious side effect between the placebo group and the Lyme Vaccine Group and then they look to see whether or not what happens long term. So we got through the 1st year, but is there any lingering potential side effects that might happen and again following people for?

NOTE Confidence: 0.935897469520569

00:27:48.400 --> 00:28:18.240 36 months after that initial trial, there did not appear to be any new issues that developed with relationship to the line vaccine. Then the issue about boosters came up where we know that you need to have high levels of the antibody around and that that drops overtime, so do you need to give a booster? How often do you have to give a booster in order to maintain that high level of antibody to protect individuals?

NOTE Confidence: 0.926663875579834

00:28:19.790 --> 00:28:48.070 The CDC came out with some recommendations on who we ought to consider and again. That's really sort of rooting out who the high risk. Individuals are in order to do that, and the other important thing to remember is the fact that in the original Lyme vaccine. Human trials that

was from 18. Two and older so there was a lot of uncertainties was it safe and effective in children.

NOTE Confidence: 0.924569725990295

00:28:48.590 --> 00:28:56.250 And there were actually trials and children that occurred afterwards that showed that it was effective and safe as well.

NOTE Confidence: 0.930426895618439

00:28:56.890 --> 00:29:22.620 But at the time that they came out with these recommendations that had not been done So what are some of the controversial issues that also were related to the Lyme vaccine and one is that in other research it was shown that when people developed arthritis in Lyme disease that they may very high titers of ASP antibodies.

NOTE Confidence: 0.944151341915131

00:29:23.820 --> 00:29:50.360 And so the question became if you're going to be giving them are there certain individuals that would be at risk developing arthritis as a result of their vaccination? Was it safe and kids? How often would we need to boost her and remember, we talked about the variability of the proteins from one species to another and if you vaccinate with will protect you against the other types of species as well.

NOTE Confidence: 0.928686916828156

00:29:52.010 --> 00:30:06.850 And lastly since we depend so much upon laboratory confirmation to diagnose Lyme disease. How is that going to impact our ability to be able to?

NOTE Confidence: 0.915497064590454

00:30:07.590 --> 00:30:09.540 To use our blood work effectively.

NOTE Confidence: 0.926080524921417

00:30:11.320 --> 00:30:25.170 And then there was the question about vaccine failures. There were certain individuals that it didn't protect and that it seemed to be in particular, the Pasteur.

NOTE Confidence: 0.926561117172241

00:30:25.700 --> 00:30:56.580 Group that individuals who are over the age of 60 were less likely to have as vigorous and immunological response against the Organism or not so one reason is that you just don't make enough of those aspray antibodies and then there was the question about out in the wild? Is there enough variability going on here that vaccinating with one aspac just wasn't going to cut it and so again this is sort of what happens when you vaccinate.

NOTE Confidence: 0.924746870994568

00:30:57.110 --> 00:31:03.820 This what they're measuring here is actually the protective antibody, which is termed LA 2.

NOTE Confidence: 0.939645290374756

00:31:04.330 --> 00:31:26.450 And what the levels were after each vaccination and then after the 12 months and what you see is you get a pretty decent response after the first two injections and then that subsides and actually drops to a level that is lower than is required for protection and then when you get that 3rd one.

NOTE Confidence: 0.929587841033936

00:31:27.820 --> 00:31:58.660 It brings the levels up even higher and then there's sort of a slower decline that happens. After that, and in those individuals who were unable to mount antibody levels above 1300. They were not adequately protected so again. There was a way to be able to measure that and that was going to factor into recommendations as to how often one would need to receive booster shots with respect.

NOTE Confidence: 0.762434124946594

00:31:58.660 --> 00:32:00.000 II wine disease.

NOTE Confidence: 0.934386789798737

00:32:01.960 --> 00:32:09.750 So we took it from the initial description sort of through some of the laboratory.

NOTE Confidence: 0.940786957740784

00:32:10.330 --> 00:32:16.160 Development on to the human trials, some of the issues that were related to the Lyme vaccine.

NOTE Confidence: 0.953151822090149

00:32:16.680 --> 00:32:22.610 And in 1998, the vaccine was approved by the FDA.

NOTE Confidence: 0.914753913879395

00:32:24.020 --> 00:32:27.370 Pasture cannot decided not to go forward with it.

NOTE Confidence: 0.946748673915863

00:32:28.150 --> 00:32:36.620 And Unfortunately due to sort of lack of interest. It was taken off of the market in 2002 because people didn't.

NOTE Confidence: 0.9366854429245

00:32:37.610 --> 00:33:03.280 Feel the need to be to have protection against Lyme disease. So we're back to our wearing are long sleeve shirts and long pants and light colored clothing and tick checks and so forth, but again, I think it's a very interesting story from a variety of different aspects. Despite the fact that it didn't it wasn't sustained.

NOTE Confidence: 0.962750196456909

00:33:04.210 --> 00:33:05.430 Thanks for your attention.

NOTE Confidence: 0.945495784282684

00:33:11.120 --> 00:33:18.610 Doctor Janine Evans is associate professor at Yale School of Madison. This was recorded on April 19th 2007.