

WEBVTT

NOTE duration:"01:01:24.738000"

NOTE language:en-us

NOTE Confidence: 0.832236170768738

00:00:00.660 --> 00:00:31.430 OK, I welcome everyone. I have the honor to introduce our speaker today. We don't know me. My name is program director for the Norwalk, and I had to pledge today introduced one of our fellow stuck to Leo Carrasco selected. Carrasco did his training. Medical school in Dominican Republic came to the United States and train internal Medicine and pulmonary at Harlem hospital affiliated with.

NOTE Confidence: 0.886213600635529

00:00:31.430 --> 00:01:02.190 On the University and then did a critical care fellowship at your hospital affiliated with Albert Einstein and we're really fortunate to have in common? Do our sleep fellowship with us so as you see doctor. Carrasco is adult pulmonary critical care physician and we have a lot of fellows that are adult training and we have a very robust pediatric program for pediatric sleep. Madison I have to tell you we take a lot of pride and it's a lot of fun when I see the adult training physicians examining their 1st.

NOTE Confidence: 0.873026788234711

00:01:02.190 --> 00:01:32.530 Pediatric patient since medical school and breaking out the old tongue depressor and looking for consuls in a 4 year old, but Doctor Crisco really took an interest in pediatric sleep. Madison with our Pediatricians in Madison Directory Doctor Lewis task and so when he decided to pick this topic. After I said it may be a good idea, he embraced it. I was really impressed. And so I think we're going for a great talk today and pediatric narcolepsy why children are not just small adults.

NOTE Confidence: 0.766632378101349

00:01:33.120 --> 00:01:37.290 I said go through those very nicely, so good afternoon.

NOTE Confidence: 0.873780012130737

00:01:40.740 --> 00:02:11.940 I would like to apologize in advance for the pediatricians since I'm not, but going over this topic in pediatric narcolepsy what I wanted to do is to make a juxtaposition with the adult in recent behind that is 'cause. I felt that in the adult narcolepsy. We have a better, more clear manifestations diagnostic tools and management.

NOTE Confidence: 0.916215419769287

00:02:12.340 --> 00:02:16.950 The pediatric population and in the pediatric population I feel that.

NOTE Confidence: 0.883669197559357

00:02:17.630 --> 00:02:26.460 They still the development process in the field of pediatric narcolepsy so I decided to go for it.

NOTE Confidence: 0.882714688777924

00:02:31.870 --> 00:02:54.840 Alright have no disclosure except that I'm not a pediatrician and I felt that why the lecture is important is because, as I just alluded to there's a marked difference in, not only the presentation, but also diagnostic tools and criteria in management for narcolepsy in both adult and pediatric population.

NOTE Confidence: 0.893344819545746

00:02:55.380 --> 00:03:26.270 So what I intend to do with the talk is to describe in this differences and make points and highlights and what are this early manifestations that were able to pick up particularly in the early stages in the children or pediatric population and then brush up on the treatment for narcolepsy, particularly in the pediatric given the fact that it is very recently of the approved the use of.

NOTE Confidence: 0.864323318004608

00:03:26.270 --> 00:03:56.950 Sodium Oxybate Siren in this in the pediatric world, so before I start. This is just one of the child age specifications. I had to go back into understanding what are the different classifications not only hbase but developmentally wise? How are we able to determine how advance a child is in their development so this is just a highlight?

NOTE Confidence: 0.685654580593109

00:03:56.950 --> 00:03:57.560 Of that.

NOTE Confidence: 0.882141590118408

00:03:58.390 --> 00:04:28.700 Then I would like to start with the case doctor. We're mentioned initially it was very nerve wracking for me to evaluate my first pediatric patient since you know, I haven't done so since medical school. But after a while. It becomes becomes becomes a skill set that I feel that it's very useful to have particularly that slipped decisions. We accept all comers. So I think that in this case, I've embraced that.

NOTE Confidence: 0.865912854671478

00:04:28.700 --> 00:04:59.140 And so my wife is also a pediatrician so I guess that that has to do something with it. But this particular case. I had the opportunity of seeing early during my fellowship, and I did want to follow up so I got very impressed with the case and what we did in her response to the treatment that we used it at the time and she's another lesson. She initially came to us because she was having works any nightmares for about 2 months and she said that.

NOTE Confidence: 0.909447193145752

00:04:59.140 --> 00:05:17.460 This episode initially had gone for years, but for the past 2 months. They became more frequent and they become more worrisome. They they were they were really scaring her so she wanted to have that evaluated In addition to that she was in the hands of.

NOTE Confidence: 0.895788490772247

00:05:18.090 --> 00:05:48.920 A therapist in a neurologist for what she was saying was difficult to concentrate and perform tasks at school and she was having this intermittent headaches, particularly in there in the early morning times and throughout the day when she was a school that would make her a difficult to do her, her daily activities at the time, her initial work up with sort of negative and choose empirically treated with the pyramid for migraines her therapist had also given her. I repeat for soul.

NOTE Confidence: 0.894679486751556

00:05:48.920 --> 00:06:19.100 Melatonin for typing in Benadryl for what she was describing was difficulty going to bad or sleeping so she said. That initially her schedule used to be very hard to fall asleep but I said, this time it was very difficult for her to stay asleep. It was easy for her to fall asleep but it was difficult to stay asleep, so they give her this regimen. It was unsuccessful and by the time, she came to us, she had associated symptoms, they associated symptoms.

NOTE Confidence: 0.814521491527557

00:06:19.100 --> 00:06:20.890 Is she had was that?

NOTE Confidence: 0.899589061737061

00:06:21.840 --> 00:06:52.730 At the time she was dragging her feet that was her description and she couldn't perform as she would usually do. She was also having this hallucinations, particularly initially visually and then they became auditory. So when she was describing is that sensation of being in bed and having the feeling of somebody looking at her or somebody being pressing in the room in initially also she was sharing the room with her little sister.

NOTE Confidence: 0.883463323116302

00:06:52.730 --> 00:07:23.520 Um in this episodes were not terrifying only for her, but her sister as well, she will ask her sister to go. Look around to see if somebody was truly there or not in the latter part of it was that then she started hearing voices in the room and that's when she started going to her bed by herself or her mother. Her parents change rooms because not only which it was difficult for her to sleep, but her little sister was also having difficulties.

NOTE Confidence: 0.89333701133728

00:07:24.650 --> 00:07:55.320 In addition to that most of the description of her daytime functioning was in school and when she would describe is that she will be in class and she would have episodes of like staring and blacking out and then thinking back like what just happened in will be difficult for her to follow the train of thought with the professor the teacher that you will have in class so her performance was taken at all, and then at night time she was also.

NOTE Confidence: 0.889637589454651

00:07:55.320 --> 00:08:20.520 Ask how you feel when you sleep there. Her description was that she was very restless. You would like every time she will have this episode. So just like tossing and turning around and back. In addition to this to say that particularly the latter part of the night when it was time for her to wake up to have episodes in which you would like wake up and feel that she cannot move so she was describing paralysis associated with that.

NOTE Confidence: 0.882706880569458

00:08:21.500 --> 00:08:52.230 In terms of negative symptoms as you're going to have any snoring. She didn't have any difficulty breathing when she was sleeping. She didn't have any episodes off of sleepwalk, although she has a brother as well, who did have episodes week. It was younger. When asked about naps. It was very interesting to me because what she was saying that she will fight the urge to nap but it was given the chance. You would map like she will fall asleep so a bunch to describe that she would not usually.

NOTE Confidence: 0.879872143268585

00:08:52.230 --> 00:09:06.060 Do gnats in terms of social history was printing significant, she was an honor student at the time and she used to do a lot of dance classes for dance dance classes.

NOTE Confidence: 0.89435601234436

00:09:06.620 --> 00:09:38.490 But since this episodes, it was very hard for her to perform. I'm terms of sleep routine. As of lately when I initially evaluated her, her bedtime is to be anywhere between 10:00 and 11:00 and she said. She didn't have a very set time to fall asleep but it will take your just a few minutes to those often fall asleep or wake up times to be variable, according to her mom. It had to be 5:45 PM alarm because of school and then when asked how did you fail upon waking up her answer was?

NOTE Confidence: 0.9211266040802

00:09:38.490 --> 00:09:47.270 I feel that I could continue to sleep and when asked how many hours of sleep should think she was getting her, her description was about 3:00 to 5:00 hours.

NOTE Confidence: 0.86941123008728

00:09:48.200 --> 00:10:18.710 Prior to this, she says that her bedtime. I used to be very regular her wake up times to be 545 she used to beat the alarm field.

Refresh machine. We can be ready to go for the day she had this very type. A personality in which she was very busy with school and her time activities in terms of bedtime. She said that by 10:00 o'clock or hit used to be in the pillow and she used to start winding down, like around nine 9:30.

NOTE Confidence: 0.870672047138214

00:10:18.710 --> 00:10:48.740 And as I mentioned that had changed dramatically by the time that that she came to us so this is a narcolepsy talk so narcolepsy was part of our differential. In addition to that. We felt that her, her total amount of hours sleep in bed was insufficient for her age group, so we recommend her to increase that sleep time and then she had other features that she was doing like using her cell phone.

NOTE Confidence: 0.825306296348572

00:10:48.740 --> 00:11:03.180 And I better electronics while in bed apart of falling asleep and she also mentioned that she was falling asleep during their so we kind of also clarify in Edgecator, about adequate sleep habits.

NOTE Confidence: 0.838609993457794

00:11:03.830 --> 00:11:29.370 Nonetheless, we went forward and perform a Apolis Innography, an multiple sleep latency test about 2:00 to 3:00 months after her initial presentation in lab policy in Agra fee was unremarkable for any conditions that would explain her presentation and her salty at the time was consistent with dark colors.

NOTE Confidence: 0.817046821117401

00:11:30.070 --> 00:11:44.520 Um so the part of the treatment and how she respond. I'll leave to the end about if anybody has any thoughts about the case or would like to add anything I accepted.

NOTE Confidence: 0.818268716335297

00:11:45.100 --> 00:11:56.250 While those enough so usually what she will say is that these episodes were happening while she was already in bed ready to fall down and why not?

NOTE Confidence: 0.599988877773285

00:11:56.960 --> 00:11:58.450 Hidden regardless messages.

NOTE Confidence: 0.853506445884705

00:12:00.620 --> 00:12:31.370 Will you convert she approves departing for the instance? Yes, so that's a really good question the way that that came about was phone contact and that happened with my attending at the time so I didn't have the chance to see her before, during the MSLT but I did after she said that she did, though her symptoms remain pretty much the same she said.

NOTE Confidence: 0.728023529052734

00:12:31.390 --> 00:12:34.190 Right.

NOTE Confidence: 0.820059299468994

00:12:34.780 --> 00:12:56.090 No, you're right right right so that doesn't really good point and through The Talk, a lot to that to the use of actigraphy slip blocks, particularly in the pediatric population in her case, we do not do it.

NOTE Confidence: 0.459174513816834

00:12:57.350 --> 00:12:59.420 But.

NOTE Confidence: 0.33386555314064

00:13:03.220 --> 00:13:03.610 No.

NOTE Confidence: 0.804711043834686

00:13:04.200 --> 00:13:16.480 Yes, she was been true for that initially ADHD generalized, anxiety and depression.

NOTE Confidence: 0.892030000686646

00:13:17.480 --> 00:13:46.250 Right so uh that's a good point. So when I saw her. I try to differentiate. Ortiz out why was new versus? What has been ongoing an what I was able to get my impression from it was that some of these symptoms. She's been dragging for a few years, but what was very clear to her was that the hypnagogic hallucinations that sleep paralysis. In the nightmares was what it was more acute in the past 2 to 3 months.

NOTE Confidence: 0.595633149147034

00:13:48.600 --> 00:13:49.310 Correct.

NOTE Confidence: 0.872407019138336

00:13:49.970 --> 00:14:19.500 So I'll start by by a definition, according to the international classification of sleep disorders. The 3rd edition. Narcolepsy is part of the subset of central disorders of Hypersomnolence is a chronic lifelong very manageable neurological disorder has 2 different types. Type one and Type 2 commonly type. One has been associated or or label ass with cataplexy attack tools without cataplexy.

NOTE Confidence: 0.856362879276276

00:14:20.110 --> 00:14:44.950 It's also a define as a hypocretin deficiency syndrome as that's part of the classification of the criteria rather to classify a type. One cataplexy in this subset Santa be associated in 70% of the cases there. 10% of type 2 that get re evaluate read diagnose or re classify as a type on because the cataplexy, either is.

NOTE Confidence: 0.87209677696228

00:14:45.600 --> 00:14:53.880 Either appears later on in the course is DCS or gets picked up or diagnose later on in the course of the Seas.

NOTE Confidence: 0.865844786167145

00:14:54.900 --> 00:15:23.260 In terms of pathophysiology is pretty much similar between the pediatric world in the adult world is a loss of hyper creating producing neurons. Hypocretin orexin is excitatory neuropeptides producing dorsal lateral hypothalamus complex is closely associated to the HLA Antigen inform. This is born. The theory or the thinking that he has an autoimmune.

NOTE Confidence: 0.852254569530487

00:15:23.840 --> 00:15:54.750 An aura autoimmune development and description or Association or ideology. Rather, although the ideologies are commonly unknown where slipped decision. So we like history so narcolepsy dates back to the late 19th century. The term narcolepsy was coined by a French physician for those French speaking people. I apologize but his name is Jamba tips.

NOTE Confidence: 0.871780276298523

00:15:54.750 --> 00:16:08.000 Jelly know if I pronounce that correctly and he had an interesting case, he had a gentleman who was around 38 years old, 39 years old. He was a winemaker at the time an?

NOTE Confidence: 0.884082019329071

00:16:08.580 --> 00:16:39.390 He was having this what what they're describing asleep attacks and then the slip attacks were happening in very specific situations, particularly when he was drinking and so when he was drinking. It was happy and with friends out. They thought he was inebriated whenever that kind of Lexia. Taxware current or whenever he was playing cards at the time is what it was called. He'll win and become very excited about winning, and then he'll have this attacks.

NOTE Confidence: 0.857801914215088

00:16:39.390 --> 00:16:52.780 So they they thought that was he was also just you know, falsely posting disk as as as an entity. I suppose that have been something intrinsically or condition that that he had.

NOTE Confidence: 0.866537690162659

00:16:53.450 --> 00:17:23.910 Uh before UM doctor Jelly know there were two other case. Reports of water. The scripts enough with the description of narcolepsy. They occur in Germany and there's actually a famous paper that was that that occur there and it was about a pathological pathological rapist and he was having excessive.

NOTE Confidence: 0.835529386997223

00:17:23.910 --> 00:17:48.970 Thoughts of like mild wrong, Thinkings and so whenever he was abused their their their victims. He'll make them seen as if he was just dozing off falling off, but they never they just put two victims over

here, so there. We just reported out in the literature and they were done by Doctor Westfall and Fisher.

NOTE Confidence: 0.879690051078796

00:17:49.830 --> 00:17:58.610 Doctor Jay Leno at the time, though, he coined the term narcolepsy. He was also he also described both type one and Type 2 later on in history.

NOTE Confidence: 0.848616003990173

00:17:59.140 --> 00:18:17.510 Is not until 3040 years later with the use of stimulants that we start treating daytime sleepiness in partially Carter Plexi at the time what they used to do is give ephedrine Intertech Lee and I used to work just partially.

NOTE Confidence: 0.861380934715271

00:18:18.090 --> 00:18:49.200 And it's not until the 1950s, which with the with the use of Poly sonography that the first case of R.E.M sleep. Add sleeve on set is described Doctor Vogel and this is the birth of the sleep monster. Rams as we have it in the criteria to describe narcolepsy later on in the 70s and 80s in Stanford in the West Coast.

NOTE Confidence: 0.0563440397381783

00:18:49.200 --> 00:18:49.900 Um.

NOTE Confidence: 0.848601877689362

00:18:50.680 --> 00:19:21.430 There was a series of doctors that that we're describing narcolepsy Indults Oricon. I models and what they did was that they had a they had a they were going on, taking dogs adopting dogs and so in part of their part of their group that they had two of the dogs had narcolepsy and they breed it out of that their offspring had narcolepsy as well.

NOTE Confidence: 0.875809371471405

00:19:21.430 --> 00:19:38.060 That was the first successful genetic transmission of narcolepsy described In addition to that during the same decades. There was also the discovery of the HLA D R&D R2, positive, particularly in patients with.

NOTE Confidence: 0.848988115787506

00:19:38.580 --> 00:20:09.730 Narcolepsy is not until the 90s and 2000s in which the actual pathophysiology is described for narcolepsy. There were 2 distinct papers that came very close together, one they will in the the the hyper creating given the name of hyper creating to Hypocretin Orexin. They both those papers had this sort of similar results. In addition to that there in the same decades.

NOTE Confidence: 0.868601024150848

00:20:09.730 --> 00:20:40.900 The in the CSF Hypocretin, one was a measure, particularly in patients with type one narcolepsy and they saw that those levels were closely undetected so that's part of the where the criteria to describe hypocretin levels in the CSF gets form is not until 2010 and up to the up-to-date that we've been focusing more particularly in the.

NOTE Confidence: 0.887461543083191

00:20:40.900 --> 00:21:12.750 Etiology diagnostic tools and management of narcolepsy and in 2009, there was a pandemic of the H1N One I'll talk a little bit more about that and how particularly Sweden and Finland. There was a spike of narcolepsy cases in patients with that. One type of the vaccine for each one and one a lot of patients also with strep throat where had an Association with narcolepsy and so that auto autoimmune reaction was also part of.

NOTE Confidence: 0.877166569232941

00:21:12.750 --> 00:21:29.120 Theory that would that still not clear, but still associated with the development of narcolepsy as a reason. I I mentioned that the FDA has approved treatment options for above excessive daytime sleepiness and cataplexy the pediatric population.

NOTE Confidence: 0.912575244903564

00:21:30.220 --> 00:22:01.090 I going over the numbers in terms of how prevalent it is in the general population here in the United States. A narcolepsy is accounts for 0.3 to 0.07% is less than 1% of the total general population when we compare that to abstract asleep that's about 9:00 to 30 times more frequent none. The less the numbers for credited centers in the United States is about 5% so, although is a condition that is rare.

NOTE Confidence: 0.870410859584808

00:22:01.090 --> 00:22:15.800 I'll say that it's not uncommon, so we're we're going to come asleep. Doctors were going to come across this condition in the pediatric population is not well studied is about half of half a percent and we compare that to abstract this new pattern is about one 4%.

NOTE Confidence: 0.901549875736237

00:22:16.530 --> 00:22:47.160 The prevalence is also associated with ethnicity the most prevalent turns to be in Asian countries, particularly Japan in China, the thinking behind that is has to do with the issue. Ledeen the lowest in Israel and in terms of a male to female ratio. The literature is variable. But there's not much of a difference. So overall this considered to have an equal distribution between males and females.

NOTE Confidence: 0.844519734382629

00:22:48.300 --> 00:23:17.870 This a grab that to me was interesting. This was the graph that represents the spike or the incidence of narcolepsy in Europe, particularly again. Finland and Sweden in there was an 8 to 12 Volt increasing

in narcolepsy at the time I had to do it was very closely associated with that with the Mona Vale in H1N, one vaccine or the Pandemrix.

NOTE Confidence: 0.898868560791016

00:23:18.400 --> 00:23:49.370 Worldwide there were other type of vaccines that not we're not edge events and so that's where the thinking that it was an autoimmune process that produced the spike at the time came about. In this paper actually look retrospectively to all of the countries and all of the population that that were vaccinated. During that and they make and this is the representation of the incidence of narcolepsy excluding.

NOTE Confidence: 0.883293092250824

00:23:49.370 --> 00:24:00.260 If in line in Sweeting and there's no there's no rise in the incidence at the time. So it's just the Association with that particular vaccine with a number of cases at the time.

NOTE Confidence: 0.884504497051239

00:24:01.720 --> 00:24:33.980 Um this slide is is very uh. I think it's the bulk of the presentation because sleepiness and children particularly in younger prepubertal school each. The children is very variable so there's no specific presentation that that they would they would have it is very tangible that is so different from adults that part of the delay in diagnosing narcolepsy.

NOTE Confidence: 0.874458134174347

00:24:33.980 --> 00:24:42.960 Particularly in the whole population comes from either misdiagnose in or under diagnosing narcolepsy at a younger each.

NOTE Confidence: 0.891377925872803

00:24:43.630 --> 00:25:14.040 And uh a lot of that I believe have to do with a that the the condition was not well known so it's rare and then be that we don't have any screening methods to be able to have it more often, or fresher in part of our differential diagnosis outside of the slip world, so having said that this is just a graphic representation of what are these manifestations of sleepiness in children so in the early age there are very?

NOTE Confidence: 0.889252126216888

00:25:14.040 --> 00:25:32.600 Hyperactive very ridable very emotional easily distracted and we just opposed that's with the adult population, as adults who tend to be more groggy more dragging our feet more. I'm not able to do this task.

NOTE Confidence: 0.894924581050873

00:25:33.180 --> 00:26:03.590 And so a lot of the this manifestation during children. Get misdiagnosed with different other conditions. Another important factor is that this kids get mislabeled with with a lot of different terminologies. One of the most common is like the hyperactivity or so they give misdiagnosed

with ADHD or they just lay scene and they can make fun of them because they're not paying much attention in Class A lot of.

NOTE Confidence: 0.876286268234253

00:26:03.590 --> 00:26:34.030 A lot of it has to do with the fact that the caregiver is the one picking up the changing and in manifestation of this sleeping in children another thing important is that in the early age of childhood. There's a lot of maps involved so part of the usual sleep recommendations that we gave us to have scheduled naps, particularly narcoleptics, so I believe that in.

NOTE Confidence: 0.884638071060181

00:26:34.030 --> 00:26:40.340 In this population is also that Gray area in which were not able to.

NOTE Confidence: 0.911285996437073

00:26:41.090 --> 00:27:13.060 Tease out or differentiate whether this is just transitioning from this page from this population of growing out of naps or they just getting better because they're napping and we consider that normal in the adult population, as I mentioned is is more is more about the negative manifestation of the condition is more about not being able to do something productivity comes down the more responsibility. We have as we become adults. It's more troublesome to perform task and.

NOTE Confidence: 0.881752669811249

00:27:13.060 --> 00:27:18.750 It becomes a burden not only for the person for the families that that their weapon so they seek help.

NOTE Confidence: 0.905467808246613

00:27:19.250 --> 00:27:50.600 When they have like, this Florida manifestation, so that's another typical differentiation between sleepiness between children and box. This was a review article made by doctor therapy and Doctor Krieger in which they data retrospective analysis of the literature at the time and they had a characterization. An impact of both the onset of symptoms of the patients versus the diagnosis and they highlight the fact that the Differentiation.

NOTE Confidence: 0.914648592472076

00:27:50.600 --> 00:27:58.420 Is about 10 or 15 years between the onset of symptoms versus work? When we're picking up the spacios particularly as adults.

NOTE Confidence: 0.871240198612213

00:27:59.070 --> 00:28:29.880 And uh this puts a burden not only in in them in our patients, but also in the health care industry because it adds to the cost of what we do, and as we can see the graph depicts this difference in early stages is where the symptoms are more Florida or when they start rather but it's not until their 30s or 40s or productive each in which there's a rise or a peek.

NOTE Confidence: 0.931516587734222

00:28:29.880 --> 00:28:31.970 In the diagnosis of this condition.

NOTE Confidence: 0.845964848995209

00:28:33.840 --> 00:29:04.590 Um in terms of strange screening tools recently also it was validated, the user of the airport sleepiness scale for children. Another lesson school. Airport chat in who there was a study done by doctor. Johns, who is the same person who validated slip into scaling adults and this, this scale. The only thing that he did was to change.

NOTE Confidence: 0.899611353874207

00:29:04.590 --> 00:29:36.030 3 items in what those 3 items were changed with the purpose of making the scale more relatable to children. Another lesson and So what they did is that they remove the alcohol portion in reference to an item 7 for the chances of falling asleep when you're sitting quietly after lunch being in the classroom as opposed to being in a public place and sitting in launcher supposed to.

NOTE Confidence: 0.88308721780777

00:29:36.030 --> 00:29:50.750 Driving a car, the conceptual framework in terms of scoring in and in the representation of sleepiness is the same. This cord that goes from zero to 24 more than time is suggested will sleep in a student at the time lesson that's considered normal.

NOTE Confidence: 0.887382984161377

00:29:52.770 --> 00:30:23.850 This is just a graphic representation of how we looks one thing of that study was that this was not in Australia and it was in the school system that it was done. It was mostly validated for children or other lesser. Rather, 12 to 18, but can also be used in the population of 7:00 and 12:00. But in the population of 7 or 12 have to be careful because you have to rely a lot on.

NOTE Confidence: 0.885079085826874

00:30:23.850 --> 00:30:46.890 On the on the either the pairing or the caregiver to give answers and so we can get give either false positive or negative results based on how well the child can describe the symptoms or or the chances of him falling asleep in this conditions or you have to rely a lot in the caregiver or the parent who's who's answering these questions.

NOTE Confidence: 0.885728061199188

00:30:48.610 --> 00:31:18.070 This is grab that I found interesting I took this graph from from an article from the New England Journal of Madison. What it depicts is that the classic representation of Plexi, particularly in the adult population is the response to a strong emotional trigger followed by weakness

that it could be in the upper portion of our body. But more class more classically in the lower portion over body.

NOTE Confidence: 0.880464017391205

00:31:18.600 --> 00:31:37.760 And uh this happens very, very I want to say frequent. I would like to say it's a very popular representation of what cataplexy is particularly in the adult population, when it comes to children.

NOTE Confidence: 0.865044414997101

00:31:38.520 --> 00:32:09.980 Uh there was a study done by doctor a classy do separate classy in Italy and I found it very interesting. It was a 10 year study in their cohort what they were doing is a they start bringing awareness to their population about what narcolepsy was and how kind of Lexie was represented and then they were they were recruiting. This children and put them in. In in a situation that would lead to.

NOTE Confidence: 0.8775794506073

00:32:09.980 --> 00:32:32.990 Particularly after but it would lead to their the cataplexy. It will lead to cataplexy or a response to a strong stimulus. They particularly used to put him on to watch TV or listen to songs that they would they would like to their their their choice. And they will do it for about 5 up to 30 minutes and then they will record them.

NOTE Confidence: 0.888365983963013

00:32:33.730 --> 00:33:02.410 And what they were able to represent was that all the neurological manifestations that that children would have in response to strong emotions so out of this, where the description of active Motors symptoms, particularly Perry oral and tongue movements facial grimaces. There were correct movements as well. In terms of the negative motor symptoms. It was more about head drops tosses tongue protrusion and facial hypotonia.

NOTE Confidence: 0.890395641326904

00:33:03.140 --> 00:33:14.020 The this pictures are just part of the representation of this symptoms that they would have in response to or how they will develop their cataplexy. I would like to.

NOTE Confidence: 0.891634523868561

00:33:14.560 --> 00:33:19.910 Take out one minute break here in a show one of those videos.

NOTE Confidence: 0.548585772514343

00:33:25.900 --> 00:33:26.640 Option.

NOTE Confidence: 0.929922819137573

00:33:28.430 --> 00:33:30.360 OK, I guess I won't be able to do so.

NOTE Confidence: 0.385570555925369

00:33:32.150 --> 00:33:33.830 The T.

NOTE Confidence: 0.857234477996826

00:33:48.630 --> 00:34:14.790 I'm sorry I was hoping for that anyhow in the video is is very graphic video and I took this from the appendix of this study, and the one of the right. It was very active motor so this child in particular start laughing and then start flailing his arms and started giggling put his tongue out.

NOTE Confidence: 0.842306077480316

00:34:15.310 --> 00:34:39.150 The one on the left would be a child will be like, laughing and then drop his hair like bobbing had one of them almost felt follow the share and they have to like go grab and so they were the 2. Most dramatic ones that that I came across from active motor symptoms and negative motor symptoms, but maybe next time.

NOTE Confidence: 0.74798309803009

00:34:40.800 --> 00:34:45.230 Yes yes.

NOTE Confidence: 0.783506333827972

00:34:45.800 --> 00:34:48.060 Correct yes.

NOTE Confidence: 0.911155939102173

00:34:48.590 --> 00:34:50.150 Yes, absolutely 100%.

NOTE Confidence: 0.819872975349426

00:34:51.770 --> 00:34:53.750 Alright so.

NOTE Confidence: 0.870190620422363

00:34:54.380 --> 00:35:25.510 To try to wrap up in terms of cataplexy. This was another landmark study that I came about. It was done by doctor. Kuhn what it was a surprise in terms of the results of the response and I say that because the initial intent of the study was to see the differences of of narcolepsy, particularly with cataplexy in the different ethnic groups and what I think the surprise was they homogeneously.

NOTE Confidence: 0.913816392421722

00:35:25.510 --> 00:36:00.080 Of the symptoms in all ethnic groups, so there was no particular ethnic groups with more subset of symptoms and presentations as opposed to another like all of them were fairly common all throughout what they were able to mark though, is the fact that the very initial symptom of narcolepsy is feeling sleepy, particularly during the data and throughout the course of their condition, particularly in adults. It could be 5 to 10 years.

NOTE Confidence: 0.878949880599976

00:36:00.080 --> 00:36:12.580 After the presentation of symptoms. They could develop narcolepsy and out of all the symptoms that they had the most disabling one was kind of place.

NOTE Confidence: 0.893388330936432

00:36:13.140 --> 00:36:44.680 And it was interesting to me when I was reading this and thinking that would make sense because children again. It's sort of in the hands of our caregiver to be able to identify or pick up with something strong. I supposed to of are in the nature of saying a something is wrong. Can you help me like children? Don't have that ability in general and as adults. I think it's more the fact that you get to appointing the burden of the disease that you can no longer take it and hence.

NOTE Confidence: 0.896153032779694

00:36:44.680 --> 00:36:57.890 You go get help so I think a lot of the presentation of narcolepsy has to do with with the ability of us to perform our daily routine orderly test.

NOTE Confidence: 0.866349399089813

00:37:00.300 --> 00:37:30.390 Um so in summary narcolepsy. It is a syndrome at least type one. It is in. We need all the tools available in our hands to be able to reach out and adequate diagnosis and what I mean by that is that though. We have to rely a lot in our clinical presentation in terms of diagnostic tools. At least for adults. We have very good set of valid atory criteria.

NOTE Confidence: 0.903021097183228

00:37:30.390 --> 00:37:47.700 But for children were lucky that we are subject in our pediatric population to the same criteria. The adult population, when it comes to the diagnostic tools that we have available to diagnose narcolepsy, particularly the multiple sleep latency test.

NOTE Confidence: 0.86324143409729

00:37:48.240 --> 00:38:19.250 The use of sleep, Locsin Actigraphy as well, and I I think there's room for improvement there and this is just a highlight of the criteria for type one narcolepsy. I did a copy and paste from the book as we can see type one. We just have 2 criteria that must be met. One of them is this irrepressible of need to sleep.

NOTE Confidence: 0.825677871704102

00:38:19.250 --> 00:38:40.940 Or take naps and he has to happen for about 3 months in the presence of either cataplexy or their missile 3 criteria to diagnose cataplexy or the presence of Hyperscript. The absence of hyper creating less than 110 apica grams per ML.

NOTE Confidence: 0.864609897136688

00:38:41.520 --> 00:39:11.670 Or less than 1/3 of the of the mean value of it. There's only 2 caveats that they make in the book about a Pediatrics and one of them is that in young children are collapsing may present as a long night sleep and that can resume when they're sleep deprived and that if type. One is strongly suspected in. We don't meet the criteria by some the MSLT. They suggest repeating DMSO check and see if you can.

NOTE Confidence: 0.869651317596436

00:39:11.670 --> 00:39:29.160 Uh uh have a positive test then an I think this comes about. But I'll touch base upon that in a couple of slides, but I think this comes about the reliability of this test and their repeat ability of this test, particularly type R Narcolepsy.

NOTE Confidence: 0.865910649299622

00:39:29.690 --> 00:40:02.200 In terms of tattoo there's more criteria, but it's it's more an exclusion criteria. If you don't meet the type one in particular, to highlight is the fact that either you. Have you have not performance yourself. Hypocretin or if you have done so that their levels are above 110. This falls into the criteria of those who the 10% that I mentioned in the beginning of the talk that if the level of CSF. Hypocretin is above that level then they can be.

NOTE Confidence: 0.733987212181091

00:40:02.200 --> 00:40:04.520 3 + 5 Type 1.

NOTE Confidence: 0.905769467353821

00:40:05.100 --> 00:40:09.830 And that there's no other condition that could explain the symptoms of the patient is presenting.

NOTE Confidence: 0.860623002052307

00:40:11.450 --> 00:40:42.140 Um so challenges so particularly in the pediatric population even though sleep, Locsin Actigraphy have been validated their most use in the research and it has been increasingly being put at, I find it a very useful tool, particularly because it's an objective measure.

NOTE Confidence: 0.911573529243469

00:40:42.140 --> 00:41:12.150 Sleep or if we if we can make that that that projection, but that representation of that child, or other lesson versus the perception of their parent their own perception of their sleep, and I think that in ruling out other conditions is also a useful tool, particularly sleep deprivation of security and disorders in the in the other lesson population in terms of the multiple sleep latency test as I mentioned earlier.

NOTE Confidence: 0.82928866147995

00:41:12.150 --> 00:41:16.120 It's not a perfect test it has a lot of.

NOTE Confidence: 0.862446188926697

00:41:16.720 --> 00:41:29.450 Uh E holes in it, and that it's always a reliable test on the reproducibility and repeatability of it. Still, the numbers are not are not great.

NOTE Confidence: 0.589939475059509

00:41:30.690 --> 00:41:32.360 I'm lastly uhm.

NOTE Confidence: 0.888341963291168

00:41:32.870 --> 00:42:03.840 The use of drug screening have something that has come about as well. There's a couple of papers that I'll show that one is for the use of it. The other is not for the use of it, but it's nothing that you know it's a strong punch into our diagnostic criteria or diagnostic tool to do again. This fits more into our pediatric patients and population as opposed to the adults because in adults and this is something that will probably.

NOTE Confidence: 0.430251777172089

00:42:03.910 --> 00:42:04.960 Credibly do.

NOTE Confidence: 0.867611110210419

00:42:05.810 --> 00:42:29.910 Uh this is just a graph that presents the use of Actigraphy, but it's mostly in research. As I mention one of the is useful because it helps us have an objective evidence of the sleep pattern of our patients help document also treatment response, particularly in the pre funeral patients.

NOTE Confidence: 0.905720353126526

00:42:30.560 --> 00:42:46.890 When when they when it has been compared with healthy control subjects is is produced good results so the evidence is there that is a useful tool for some reason we don't use it as much in our clinical clinical setting.

NOTE Confidence: 0.840929627418518

00:42:48.060 --> 00:43:18.610 In terms of the MSLT this one of the papers that I came about that. The validates the use of it, particularly in the in the in the pediatric population in it was a study that was done by Doctor Pizza Company in which they they took patients not only would type one. But with Type 2 narcolepsy and they took all comments. They they had, and they have children.

NOTE Confidence: 0.864591896533966

00:43:18.610 --> 00:43:49.700 Although the population of children that they had. I was small but they still try to explore the reliability and repeatability of the test in that population and the results were good in the sense that particularly Type 1. You're able to repeat. There's a consistency. And when you do an MSLT and the chances of becoming staying positive in patients with.

NOTE Confidence: 0.833987951278687

00:43:49.700 --> 00:43:56.640 Type corner collapse, E or having a negative study and they're having a positive one to make their diagnosis is greater.

NOTE Confidence: 0.868083238601685

00:43:57.510 --> 00:44:08.300 And I think their their inclusion criteria was worth very strict for the study. So it's something that you know to keep in mind.

NOTE Confidence: 0.884846925735474

00:44:09.890 --> 00:44:14.240 Terms of drug screen. This is the two studies that I alluded to the first one.

NOTE Confidence: 0.831648647785187

00:44:15.030 --> 00:44:40.160 Uh was done in Boston, the one at the bottom was done in Ohio and the results were very different. The first study? What show was that in all the patients that they did MSLT. They did drug screen and all the drug screen was negative in all deals charger, so they recommend not to routinely use your interest.

NOTE Confidence: 0.873728513717651

00:44:40.720 --> 00:45:05.620 The one at the bottom and the other had it was the complete opposite like, at least 30 to 40%. If I recall correctly of all their drugs test prior to the MSLT became either positive to marijuana or on Phantom. It's so they recommend for the use of routine drug screening, particularly before Emma salty.

NOTE Confidence: 0.863311171531677

00:45:06.700 --> 00:45:18.470 The ASM on the other hand, uh in in their guidelines. Uh they have it as an option so they they they don't vouch for or against.

NOTE Confidence: 0.877384662628174

00:45:21.740 --> 00:45:52.090 So, in terms of research. I think the two one of the 2 most used tools is the HLA and the levels of hyper creating in the CSF is very well established their use. There's a strong Association between the 2:00 and I think that is an important way of Validating, the diagnosis of narcolepsy.

NOTE Confidence: 0.890102326869965

00:45:52.090 --> 00:46:05.900 But you know, there there are one of them is an invasive procedure requires a lumbar puncture and then the other one that most closely associated has been only with type one narcoleptics so.

NOTE Confidence: 0.874446570873261

00:46:07.690 --> 00:46:39.270 OK, lastly in terms of Management in terms of treatment for narcolepsy at this time in the pediatric population. There is no evidence base or consensus guidelines for that as I mention it has recently been approved the use of siding oxybate in both our collapse, E with excessive daytime

sleepiness and cataplexy and I'll go over this study. This is an algorithm that I created 2.

NOTE Confidence: 0.869953453540802

00:46:39.270 --> 00:46:59.710 Have a clear understanding of the treatment approach of Peach is an if a patient comes and they have cataplexy. These are the options that we should have down to the presence. Tissiers an SSR eyes have been there for quite some time as I showed in my history slide.

NOTE Confidence: 0.863515257835388

00:47:00.560 --> 00:47:14.980 And then um there is there's a certain oppositely siram in terms of the excessive daytime sleepiness. We have CNS stimulants and wait for motor medication, which are very well tolerated very well use as well.

NOTE Confidence: 0.87860769033432

00:47:16.060 --> 00:47:46.570 Um so this was the the trial done by jazz, Pharmaceuticals or sponsored by just from Pharmaceuticals. It was prospective double blind placebo controlled. Randomized withdraw multisite study an open label. So it's it's a mouthful but it was also a complicated started. I find it in the age range that they have was between 7:00 to 16 years old.

NOTE Confidence: 0.854332327842712

00:47:46.570 --> 00:48:08.450 Uh they had a narcolepsy with cataplexy. They took patients who were also neither stimulants or wake promoting medication and what they did was that they also took patients who were who had the diagnosis of narcolepsy and we're naive entry.

NOTE Confidence: 0.849886357784271

00:48:09.110 --> 00:48:39.610 Those who who had narcolepsy and we're inserting observation was were also screen and enrolled in the study what they did was that in this uh screen period or or they call it the Open label titration period. Those who were on a stable. Those who were on and wondering stable, though, so they kept them for at least 3 weeks. Those who were naive to the to the medication. They were titrating them up wait base.

NOTE Confidence: 0.853878796100616

00:48:39.610 --> 00:49:09.700 Up until they were stable for 2 weeks. If I make any mistakes. Can you correctly please. Thank you so after that, after they were on this table those they went onto randomized patients so the randomization in the way that I see it was that they had two arms and within that warms. They had another terms, so the 1st is between those who were going to get the Open Label Sodium Oxybate versus those who were going to get either the sodium oxybate versus placebo.

NOTE Confidence: 0.863637447357178

00:49:09.700 --> 00:49:10.570 And so.

NOTE Confidence: 0.863725364208221

00:49:11.190 --> 00:49:21.080 After they they completed 2 weeks on on on on those arms, then everybody one into the Open Label Sodium Oxybate.

NOTE Confidence: 0.851494431495667

00:49:21.710 --> 00:49:49.760 The lab that those 2 tables that I have is just a representation of how they did. The titration again. It was weight based the lowest dose over was less than 2 gram the end was to simile adult population to aim for 9 grams per night total or 6 based on weight in in terms of age. Each group ethnicity and sex it was pretty even.

NOTE Confidence: 0.894459128379822

00:49:51.620 --> 00:50:10.320 In terms of of uh the different tools that they had for assess for response. They were 2 primary endpoint ones. One was the CGI see which is the classification the global classification.

NOTE Confidence: 0.676828324794769

00:50:11.120 --> 00:50:14.770 I'm blanking on sorry.

NOTE Confidence: 0.66699093580246

00:50:15.530 --> 00:50:17.340 Yes.

NOTE Confidence: 0.898573517799377

00:50:19.700 --> 00:50:27.420 I apologize so this is a scale that is used to determine the response of treatment to cataplexy.

NOTE Confidence: 0.868399024009705

00:50:28.270 --> 00:50:50.190 And uh what they what they do is that it's a self reported a scale in the first graph representing is the blue line represents those patients who are possible. The one on the right lines represents those where on sodium oxybate an between the 2:00.

NOTE Confidence: 0.870411098003387

00:50:51.000 --> 00:51:22.180 What they are representing is the number. The median number of cataplexy attacks for weeks and as you can see there's a clear difference between those who were uncertain boxer versus those who are not the caveat to that is the second graph to the right side in which the first column. The pics plus single arm in which they were describing whether or not they they felt better or they felt worse.

NOTE Confidence: 0.866506338119507

00:51:22.180 --> 00:51:25.050 Or there was no change and then.

NOTE Confidence: 0.871920108795166

00:51:26.020 --> 00:51:47.240 About 66% of them who were in the placebo felt much worse off the drug in terms of those who were on the sodium oxybate arm which is the far right column there. Only 17% of Dunn said that they felt just about much worse or worse than what they were.

NOTE Confidence: 0.884087324142456

00:51:47.880 --> 00:51:55.810 So there's a clear change in the way that these patients were failing on plus evil versus drug.

NOTE Confidence: 0.847160756587982

00:51:56.490 --> 00:52:26.700 In terms of the Epworth Sleepiness scale. The one that the scale that they used was the children. Another lesson scale. This was the 2nd secondary end point in this one. The first table? What is representing is there scored based on a stable on the stable dose so this arm is to pursue arm. This is the sodium oxybate arm and the change from baseline.

NOTE Confidence: 0.819346189498901

00:52:26.700 --> 00:52:45.790 Was not uh uh uh? Well was somewhat significant? Which was a 3 based on the pursuer supposed to to the sodium oxybate. The caveat to that is that they did a subgroup analysis and that change was no longer pressing so there.

NOTE Confidence: 0.892603099346161

00:52:46.450 --> 00:53:11.740 The the thinking is that this has something to do with the fact that these patients were also on a form or either. Stimulants are awake promoter medication that could affect the results of of the of their response nonetheless. The median change. It's in the graph on the far left there is some variability there.

NOTE Confidence: 0.336231410503387

00:53:12.340 --> 00:53:16.830 An A in an?

NOTE Confidence: 0.936126470565796

00:53:17.460 --> 00:53:20.780 Again, it's it's not it's not a strong point of the study.

NOTE Confidence: 0.816735744476318

00:53:22.610 --> 00:53:26.440 In terms of adverse events.

NOTE Confidence: 0.903446078300476

00:53:26.990 --> 00:53:38.820 When I when I saw the list of adverse events. It was pretty much the same or very similar to the same adverse events that adults complain about in this case.

NOTE Confidence: 0.907375156879425

00:53:39.710 --> 00:54:08.340 There were only 2 cases one of acute psychosis and another one was suicidal and they actually took him out of the study that were the most critical adverse events that I was able to come across in this particular group of the majority of them who were listed either. GI side effects or weight changes or this and S were very tolerable so they were able to continue the drug without much difficulty.

NOTE Confidence: 0.61553829908371

00:54:08.840 --> 00:54:10.240 But the greatest immigrants.

NOTE Confidence: 0.887506544589996

00:54:11.810 --> 00:54:19.420 About 50% of the population of the of the those who are enrolled where own a form of either stimulus or work for motor medication.

NOTE Confidence: 0.800255060195923

00:54:20.520 --> 00:54:38.430 So this is 2 by 2 table that that when one or 2 by 2:00, but it's a table that I made to compare prior trials that have done studies study Max Abating adults versus those in Pediatrics, Ann.

NOTE Confidence: 0.877873957157135

00:54:39.180 --> 00:55:10.430 The only thing that that there are they all say that was majorly different is that in the sodium. Oxybate trials in adults. They had a more objective way of looking for different changes in the patient's symptoms or improvement. They were in that policy of Nogra Fi MWTS&MSLT's supposed to the pediatric that was purely more subjective.

NOTE Confidence: 0.886856138706207

00:55:10.430 --> 00:55:15.100 Of way of and self report ways of saying how they feel.

NOTE Confidence: 0.877285659313202

00:55:15.680 --> 00:55:45.990 In terms of the groups or the types of narcoleptics that were involved in the case. It was pretty much similar and then as I mentioned the adverse events were also very similar so what's in the pipeline. Unfortunately for the pediatric population. There's not much out there in terms of what's common in aside from sodium oxybate, but Allison is estimated inverse of each 3 receptor.

NOTE Confidence: 0.883640706539154

00:55:45.990 --> 00:56:12.030 Um and there's a study that opened in Europe. They're not enrolling yet and there, trying to look at both patients with narcolepsy. But with narcolepsy with and without cataplexy in terms of hyper creating and soul around for tall, there, only in the adult population, there, I don't think there any results out as the most recent trials that they've done but it's something to look forward to.

NOTE Confidence: 0.885083317756653

00:56:12.540 --> 00:56:34.620 I put the slide out because I find it very important to highlight the awareness of narcolepsy and I think particularly this. Two groups and networks wake up narcolepsy and they're not collapsing network are doing a good job until bringing that awareness not only 2.

NOTE Confidence: 0.899450957775116

00:56:35.570 --> 00:56:53.050 The medical field but the 2:00 the general population. I think it's a good reach that needs to occur, particularly in schools or educational systems because it's something that I mentioned even though it's rare is not uncommon.

NOTE Confidence: 0.877953052520752

00:56:53.620 --> 00:57:24.430 So having said that I'll I'll digress back to our case. We started treatment for narcolepsy. We gave her some oxybate initially and then you still feeling tired and exhausted during the day so we started arm with that. For now, with the combination of tools. You had a marked improvement of her symptoms. She became more her performance, particularly school increased.

NOTE Confidence: 0.86365270614624

00:57:24.430 --> 00:57:40.710 Um she in subsequent basis notice the difference between how she was versus how she is now the nightmares and sleep paralysis. Episodes had disappear as she did report some GI side effects such as like.

NOTE Confidence: 0.884425044059753

00:57:41.250 --> 00:57:45.590 Nauseous vomiting, but she said that they were they were tolerable.

NOTE Confidence: 0.899827659130096

00:57:46.250 --> 00:58:16.340 So you know, she she did well, um, she's happy, she's back to the owners owner on our group in her class. So to me was it was rewarding to have seen that progress in conclusion. What I would like to stress again is that there is variability in the presentation of excessive daytime sleepiness in children and adults that we still have ways to go in a lot of challenges in terms of diagnostic modality treatment.

NOTE Confidence: 0.859368443489075

00:58:16.340 --> 00:58:22.380 Actions are although right now, the only thing that we have at the area proof is sodium oxybate or siren.

NOTE Confidence: 0.905808448791504

00:58:23.070 --> 00:58:34.020 There there other medications that are in the pipeline potentially for the pediatric population as well, and we're looking forward to future therapies.

NOTE Confidence: 0.80138486623764

00:58:34.620 --> 00:58:37.730 Thank you.

NOTE Confidence: 0.829392433166504

00:58:41.960 --> 00:58:51.630 So we have some probably at the end of the hour, but if anybody would like to say that any questions.

NOTE Confidence: 0.691801428794861

00:58:55.910 --> 00:58:58.180 How much was the doors?

NOTE Confidence: 0.791241824626923

00:59:00.430 --> 00:59:02.480 Is weight based Lumia for children?

NOTE Confidence: 0.770325362682343

00:59:03.410 --> 00:59:10.670 Oh, so for her, I believe we reach a 9 grams, Yes total total.

NOTE Confidence: 0.860992252826691

00:59:11.680 --> 00:59:38.560 She's doing that damn left no yes. Yes, we started out at the lower dose and then we were titrated her up and then we even had to switch the amount of those she was taking the 2 doses 'cause. She said that she was waking up to retire. So I think we give her a little bit more in the first those before going to bed into the second. Those were kind of cut down but the total the total amount that she came on requirement was not.

NOTE Confidence: 0.872240662574768

00:59:41.170 --> 00:59:46.840 So typically not not see we always ask about you know your high school and you had a lesson.

NOTE Confidence: 0.821545004844666

00:59:47.610 --> 01:00:18.390 Yeah, I would support that actually it would be in elementary school let you see yes. So yes, that's a good point. So most again. Most of the changes. Both behavior and their symptoms. That's exactly when they appear early early in life in the elementary period, an A lot of the papers what they put stresses.

NOTE Confidence: 0.9032381772995

01:00:18.390 --> 01:00:42.850 Is that the ones who are uh that once were identifying these children are the caregivers and so they see it shift between their behavior and their performance versus how they were, and that's what that's what they attention comes about and a lot of those children they either get. They stay under the radar misdiagnosed because they they get misdiagnosed or something else.

NOTE Confidence: 0.641189098358154

01:00:43.490 --> 01:00:51.910 I'm done come to us and your patience.

NOTE Confidence: 0.764831840991974

01:00:52.530 --> 01:00:58.450 She stopped at the paramount as well. The only regulation stayed on West was it was this tire man.

NOTE Confidence: 0.396875709295273

01:00:59.410 --> 01:00:59.940 English.

NOTE Confidence: 0.847927749156952

01:01:04.060 --> 01:01:05.940 Alright alright really good thank you.

NOTE Confidence: 9.04565240489319E-05

01:01:13.080 --> 01:01:21.540 I.

NOTE Confidence: 0.186173230409622

01:01:22.110 --> 01:01:24.710 So.