

WEBVTT

NOTE duration:"00:15:25"

NOTE recognizability:0.672

NOTE language:en-us

NOTE Confidence: 0.871461388571429

00:00:16.650 --> 00:00:18.535 Welcome back, this session is

NOTE Confidence: 0.871461388571429

00:00:18.535 --> 00:00:19.730 being recorded. Thank you.

NOTE Confidence: 0.897359285933333

00:00:22.520 --> 00:00:24.686 Hello, it's my pleasure now to

NOTE Confidence: 0.897359285933333

00:00:24.686 --> 00:00:26.566 introduce our next speaker Dean

NOTE Confidence: 0.897359285933333

00:00:26.566 --> 00:00:28.431 Yumemi who is assistant professor

NOTE Confidence: 0.897359285933333

00:00:28.431 --> 00:00:30.853 in the Department of Pediatrics and

NOTE Confidence: 0.897359285933333

00:00:30.853 --> 00:00:33.003 the Director of Pediatric Hepatology

NOTE Confidence: 0.897359285933333

00:00:33.003 --> 00:00:35.362 Research at Yale School of Medicine

NOTE Confidence: 0.897359285933333

00:00:35.362 --> 00:00:38.529 and his topic today is going to be

NOTE Confidence: 0.897359285933333

00:00:38.529 --> 00:00:40.969 investigative pediatric hepatology Dean.

NOTE Confidence: 0.345161611

00:00:43.650 --> 00:00:47.298 Sharing my screen.

NOTE Confidence: 0.345161611

00:00:47.300 --> 00:00:49.292 Thanks a lot Michael for introducing

NOTE Confidence: 0.345161611

00:00:49.292 --> 00:00:52.000 me thanks to the organizing committee.

NOTE Confidence: 0.345161611

00:00:52.000 --> 00:00:54.272 Mario, Michael Nathanson, Dr.
NOTE Confidence: 0.345161611

00:00:54.272 --> 00:00:56.280 Boyer, for just giving me
NOTE Confidence: 0.345161611

00:00:56.280 --> 00:00:59.092 a little bit of time as a,
NOTE Confidence: 0.345161611

00:00:59.092 --> 00:01:00.608 you know, as a pediatrician,
NOTE Confidence: 0.345161611

00:01:00.610 --> 00:01:03.715 as a as a pediatric gastrologist
NOTE Confidence: 0.345161611

00:01:03.715 --> 00:01:07.278 hepatologist I've been asked to talk about
NOTE Confidence: 0.345161611

00:01:07.278 --> 00:01:08.245 investigative pediatric, hepatology,
NOTE Confidence: 0.345161611

00:01:08.245 --> 00:01:10.520 and my subtitle is where we've been
NOTE Confidence: 0.345161611

00:01:10.520 --> 00:01:12.747 where we are and where we're going,
NOTE Confidence: 0.345161611

00:01:12.750 --> 00:01:17.014 and in preparation to talk to you today,
NOTE Confidence: 0.345161611

00:01:17.020 --> 00:01:18.838 I actually pulled a number of
NOTE Confidence: 0.345161611

00:01:18.838 --> 00:01:20.411 my colleagues from around the
NOTE Confidence: 0.345161611

00:01:20.411 --> 00:01:22.205 country just to get an impression.
NOTE Confidence: 0.345161611

00:01:22.210 --> 00:01:23.740 You know, from different places
NOTE Confidence: 0.345161611

00:01:23.740 --> 00:01:24.964 and and different people,
NOTE Confidence: 0.345161611

00:01:24.970 --> 00:01:26.550 both on the West Coast, Midwest,

NOTE Confidence: 0.345161611

00:01:26.550 --> 00:01:29.070 several people here on the East Coast,

NOTE Confidence: 0.345161611

00:01:29.070 --> 00:01:31.476 about, you know what are the

NOTE Confidence: 0.345161611

00:01:31.476 --> 00:01:33.990 the real problems in pediatric

NOTE Confidence: 0.345161611

00:01:33.990 --> 00:01:35.950 hepatology that have been?

NOTE Confidence: 0.345161611

00:01:35.950 --> 00:01:38.230 Assured and the ones that have

NOTE Confidence: 0.345161611

00:01:38.230 --> 00:01:40.552 gotten better and ones that we

NOTE Confidence: 0.345161611

00:01:40.552 --> 00:01:42.780 wish we had better solutions for.

NOTE Confidence: 0.345161611

00:01:42.780 --> 00:01:43.538 And remarkably,

NOTE Confidence: 0.345161611

00:01:43.538 --> 00:01:44.296 you know,

NOTE Confidence: 0.345161611

00:01:44.296 --> 00:01:46.191 although there are some differences

NOTE Confidence: 0.345161611

00:01:46.191 --> 00:01:47.833 between you know those who

NOTE Confidence: 0.345161611

00:01:47.833 --> 00:01:49.343 practice in Los Angeles versus

NOTE Confidence: 0.345161611

00:01:49.343 --> 00:01:51.237 those who practice in Saint Louis.

NOTE Confidence: 0.345161611

00:01:51.240 --> 00:01:53.360 A lot of the problems that they see

NOTE Confidence: 0.345161611

00:01:53.360 --> 00:01:55.157 across the country are the same.

NOTE Confidence: 0.345161611

00:01:55.160 --> 00:01:56.928 The questions that I talked to them about,

NOTE Confidence: 0.345161611

00:01:56.930 --> 00:01:58.322 and I'm going to.

NOTE Confidence: 0.345161611

00:01:58.322 --> 00:02:00.970 We're going to talk about a couple

NOTE Confidence: 0.345161611

00:02:00.970 --> 00:02:03.060 of vignettes about things that

NOTE Confidence: 0.345161611

00:02:03.060 --> 00:02:04.660 came up in our conversation.

NOTE Confidence: 0.345161611

00:02:04.660 --> 00:02:06.650 I asked them in the last five to 10 years.

NOTE Confidence: 0.345161611

00:02:06.650 --> 00:02:08.426 That and scientific improvements

NOTE Confidence: 0.345161611

00:02:08.426 --> 00:02:11.664 have made it a significant impact in

NOTE Confidence: 0.345161611

00:02:11.664 --> 00:02:13.656 your clinical hepatology practice.

NOTE Confidence: 0.345161611

00:02:13.660 --> 00:02:14.548 You know,

NOTE Confidence: 0.345161611

00:02:14.548 --> 00:02:17.212 have there are there conceptual or

NOTE Confidence: 0.345161611

00:02:17.212 --> 00:02:19.555 technical hurdles that you know you

NOTE Confidence: 0.345161611

00:02:19.555 --> 00:02:22.137 wish we could get through that could

NOTE Confidence: 0.345161611

00:02:22.137 --> 00:02:24.357 improve your current practice and

NOTE Confidence: 0.345161611

00:02:24.357 --> 00:02:26.776 you know what diseases are going

NOTE Confidence: 0.345161611

00:02:26.776 --> 00:02:29.320 to still be with us in five years,

NOTE Confidence: 0.345161611

00:02:29.320 --> 00:02:32.836 and what diseases seem to be

NOTE Confidence: 0.345161611

00:02:32.836 --> 00:02:34.594 increasing in prevalence.

NOTE Confidence: 0.345161611

00:02:34.600 --> 00:02:36.050 So we're going to have.

NOTE Confidence: 0.345161611

00:02:36.050 --> 00:02:37.751 I'm going to talk about 3 quick

NOTE Confidence: 0.345161611

00:02:37.751 --> 00:02:39.112 vignettes and each of them start

NOTE Confidence: 0.345161611

00:02:39.112 --> 00:02:40.780 with a a quote from one of the

NOTE Confidence: 0.345161611

00:02:40.780 --> 00:02:42.322 hepatologists that I talked to and

NOTE Confidence: 0.345161611

00:02:42.322 --> 00:02:43.976 then the first one was this that

NOTE Confidence: 0.345161611

00:02:43.976 --> 00:02:45.765 this is the bread and butter of

NOTE Confidence: 0.345161611

00:02:45.765 --> 00:02:47.019 pediatric transplant hepatology,

NOTE Confidence: 0.345161611

00:02:47.020 --> 00:02:49.232 and it still will be a major

NOTE Confidence: 0.345161611

00:02:49.232 --> 00:02:51.288 problem for us in five years.

NOTE Confidence: 0.345161611

00:02:51.290 --> 00:02:55.070 You know, as pediatricians we see.

NOTE Confidence: 0.345161611

00:02:55.070 --> 00:02:55.994 At birth,

NOTE Confidence: 0.345161611

00:02:55.994 --> 00:02:58.766 yellow babies very very commonly and

NOTE Confidence: 0.345161611

00:02:58.766 --> 00:03:01.514 the differential is quite broad.
NOTE Confidence: 0.345161611

00:03:01.514 --> 00:03:05.610 The 1st 2 on this list of differential
NOTE Confidence: 0.345161611

00:03:05.610 --> 00:03:08.574 are the most common and sometimes
NOTE Confidence: 0.345161611

00:03:08.574 --> 00:03:11.901 when you get to more serious
NOTE Confidence: 0.345161611

00:03:11.901 --> 00:03:13.776 hepatology focused diagnosis
NOTE Confidence: 0.345161611

00:03:13.776 --> 00:03:17.809 it it causes a delay in care.
NOTE Confidence: 0.345161611

00:03:17.810 --> 00:03:21.062 But most children who are born
NOTE Confidence: 0.345161611

00:03:21.062 --> 00:03:23.230 in neonates have physiologic
NOTE Confidence: 0.345161611

00:03:23.230 --> 00:03:25.180 jaundice because of the transition.
NOTE Confidence: 0.345161611

00:03:25.180 --> 00:03:27.928 Between going from inside to outside,
NOTE Confidence: 0.345161611

00:03:27.930 --> 00:03:30.666 there is some association with breastfeeding,
NOTE Confidence: 0.345161611

00:03:30.670 --> 00:03:32.847 jaundice and you know if they need
NOTE Confidence: 0.345161611

00:03:32.847 --> 00:03:34.146 a little phototherapy that'll
NOTE Confidence: 0.345161611

00:03:34.146 --> 00:03:35.390 get them through it,
NOTE Confidence: 0.345161611

00:03:35.390 --> 00:03:38.102 but for those who have actually
NOTE Confidence: 0.345161611

00:03:38.102 --> 00:03:39.006 conjugated hyperbilirubinemia,

NOTE Confidence: 0.345161611

00:03:39.010 --> 00:03:40.186 you know there are.

NOTE Confidence: 0.345161611

00:03:40.186 --> 00:03:41.656 There's a list of things,

NOTE Confidence: 0.345161611

00:03:41.660 --> 00:03:44.642 and the most common thing that I'll

NOTE Confidence: 0.345161611

00:03:44.642 --> 00:03:47.968 touch on which that Hepatologist said,

NOTE Confidence: 0.345161611

00:03:47.970 --> 00:03:51.416 is his bread and butter is biliary atresia.

NOTE Confidence: 0.345161611

00:03:51.416 --> 00:03:54.650 If you're not familiar with biliary atresia,

NOTE Confidence: 0.345161611

00:03:54.650 --> 00:03:56.366 it's basically a fibroscan.

NOTE Confidence: 0.345161611

00:03:56.366 --> 00:03:58.511 We're seeing disease of the

NOTE Confidence: 0.345161611

00:03:58.511 --> 00:04:00.348 extra hepatic bile ducts,

NOTE Confidence: 0.345161611

00:04:00.350 --> 00:04:02.395 although it's known that it

NOTE Confidence: 0.345161611

00:04:02.395 --> 00:04:04.440 can actually at times affect

NOTE Confidence: 0.825598331142857

00:04:04.514 --> 00:04:06.558 the intrahepatic bile ducts,

NOTE Confidence: 0.825598331142857

00:04:06.560 --> 00:04:08.674 and that there's a variety of causes,

NOTE Confidence: 0.825598331142857

00:04:08.680 --> 00:04:09.704 it's multifactorial.

NOTE Confidence: 0.825598331142857

00:04:09.704 --> 00:04:12.264 There's no one specific cause,

NOTE Confidence: 0.825598331142857

00:04:12.270 --> 00:04:13.746 and you know there are many
NOTE Confidence: 0.825598331142857

00:04:13.746 --> 00:04:15.290 models that have been developed,
NOTE Confidence: 0.825598331142857

00:04:15.290 --> 00:04:19.090 both viral models, toxic models.
NOTE Confidence: 0.825598331142857

00:04:19.090 --> 00:04:21.440 There are known genetic causes,
NOTE Confidence: 0.825598331142857

00:04:21.440 --> 00:04:23.816 and as a result we actually
NOTE Confidence: 0.825598331142857

00:04:23.816 --> 00:04:26.574 know quite a bit about things.
NOTE Confidence: 0.825598331142857

00:04:26.574 --> 00:04:30.318 That that can cause biliary atresia.
NOTE Confidence: 0.825598331142857

00:04:30.320 --> 00:04:32.720 There can be children who are born at
NOTE Confidence: 0.825598331142857

00:04:32.720 --> 00:04:35.424 birth with the form of biliary trees
NOTE Confidence: 0.825598331142857

00:04:35.424 --> 00:04:37.459 with fibrosis and significant jaundice,
NOTE Confidence: 0.825598331142857

00:04:37.460 --> 00:04:41.080 but the most common causes of biliary
NOTE Confidence: 0.825598331142857

00:04:41.080 --> 00:04:43.240 atresia seem to happen after birth,
NOTE Confidence: 0.825598331142857

00:04:43.240 --> 00:04:45.907 and it's not clear you know what
NOTE Confidence: 0.825598331142857

00:04:45.907 --> 00:04:48.100 exactly is causing these things.
NOTE Confidence: 0.825598331142857

00:04:48.100 --> 00:04:51.124 It it likely is a combination of of
NOTE Confidence: 0.825598331142857

00:04:51.124 --> 00:04:54.300 genes as well as viruses and toxins,

NOTE Confidence: 0.825598331142857
00:04:54.300 --> 00:04:56.838 but what is known is that
NOTE Confidence: 0.825598331142857
00:04:56.838 --> 00:04:58.107 there's a significant.
NOTE Confidence: 0.825598331142857
00:04:58.110 --> 00:05:01.236 Response by the immune system where
NOTE Confidence: 0.825598331142857
00:05:01.236 --> 00:05:03.913 the epithelium and fibroblasts in
NOTE Confidence: 0.825598331142857
00:05:03.913 --> 00:05:06.478 biliary ducts actually respond pretty
NOTE Confidence: 0.825598331142857
00:05:06.478 --> 00:05:09.839 significantly and in the last 15 to 20
NOTE Confidence: 0.825598331142857
00:05:09.839 --> 00:05:12.674 years I made that go away 15 to 20 years.
NOTE Confidence: 0.825598331142857
00:05:12.674 --> 00:05:13.166 You know,
NOTE Confidence: 0.825598331142857
00:05:13.170 --> 00:05:16.908 we understand much more about the.
NOTE Confidence: 0.825598331142857
00:05:16.910 --> 00:05:17.572 The contribution,
NOTE Confidence: 0.825598331142857
00:05:17.572 --> 00:05:20.220 both of the immune system as well as
NOTE Confidence: 0.825598331142857
00:05:20.281 --> 00:05:23.421 the fibrotic component that starts it.
NOTE Confidence: 0.825598331142857
00:05:23.421 --> 00:05:26.406 But you know Despite that.
NOTE Confidence: 0.825598331142857
00:05:26.410 --> 00:05:28.377 You know and and using immune suppression,
NOTE Confidence: 0.825598331142857
00:05:28.380 --> 00:05:31.240 we haven't made a significant
NOTE Confidence: 0.825598331142857

00:05:31.240 --> 00:05:35.144 impact on actually reducing the the
NOTE Confidence: 0.825598331142857

00:05:35.144 --> 00:05:38.056 need for surgical intervention.
NOTE Confidence: 0.825598331142857

00:05:38.060 --> 00:05:40.598 A number of studies this is 1 by Georgie
NOTE Confidence: 0.825598331142857

00:05:40.598 --> 00:05:42.420 Pizzera at Cincinnati Children's.
NOTE Confidence: 0.825598331142857

00:05:42.420 --> 00:05:44.650 Put everyone on steroids after
NOTE Confidence: 0.825598331142857

00:05:44.650 --> 00:05:46.434 surgical intervention for BA.
NOTE Confidence: 0.825598331142857

00:05:46.440 --> 00:05:49.068 They saw minimal if any impact
NOTE Confidence: 0.825598331142857

00:05:49.068 --> 00:05:51.899 when they put children on steroids.
NOTE Confidence: 0.825598331142857

00:05:51.900 --> 00:05:53.888 What they did see is that there
NOTE Confidence: 0.825598331142857

00:05:53.888 --> 00:05:55.280 was increased biliary drainage.
NOTE Confidence: 0.825598331142857

00:05:55.280 --> 00:05:56.243 What was actually?
NOTE Confidence: 0.825598331142857

00:05:56.243 --> 00:05:58.490 More important in this study is that
NOTE Confidence: 0.825598331142857

00:05:58.553 --> 00:06:00.539 when you put children on steroids,
NOTE Confidence: 0.825598331142857

00:06:00.540 --> 00:06:02.694 a significant proportion in under 30
NOTE Confidence: 0.825598331142857

00:06:02.694 --> 00:06:04.709 days actually developed a a signal.
NOTE Confidence: 0.825598331142857

00:06:04.710 --> 00:06:05.647 First,

NOTE Confidence: 0.825598331142857
00:06:05.647 --> 00:06:11.269 a severe event such as sepsis
NOTE Confidence: 0.825598331142857
00:06:11.270 --> 00:06:13.474 or other surgical intervention
NOTE Confidence: 0.825598331142857
00:06:13.474 --> 00:06:16.780 causing the cessation of the this
NOTE Confidence: 0.825598331142857
00:06:16.869 --> 00:06:19.335 this trial now you know,
NOTE Confidence: 0.825598331142857
00:06:19.335 --> 00:06:22.545 although we know quite a bit
NOTE Confidence: 0.825598331142857
00:06:22.545 --> 00:06:25.539 about potential mechanisms.
NOTE Confidence: 0.825598331142857
00:06:25.540 --> 00:06:29.899 There are delays in identification if
NOTE Confidence: 0.825598331142857
00:06:29.899 --> 00:06:31.813 we could have a better understanding
NOTE Confidence: 0.825598331142857
00:06:31.813 --> 00:06:34.111 of what some of the mechanistic
NOTE Confidence: 0.825598331142857
00:06:34.111 --> 00:06:36.655 understanding using maybe some of the
NOTE Confidence: 0.825598331142857
00:06:36.655 --> 00:06:38.678 technologies that are out there today.
NOTE Confidence: 0.825598331142857
00:06:38.680 --> 00:06:40.846 Single cell sequencing is one that's
NOTE Confidence: 0.825598331142857
00:06:40.846 --> 00:06:42.999 being applied to to this area.
NOTE Confidence: 0.825598331142857
00:06:43.000 --> 00:06:47.130 We could probably develop better.
NOTE Confidence: 0.825598331142857
00:06:47.130 --> 00:06:49.514 Targeted therapies for children
NOTE Confidence: 0.825598331142857

00:06:49.514 --> 00:06:53.090 with with BA but currently whoops.
NOTE Confidence: 0.825598331142857

00:06:53.090 --> 00:06:56.154 I lost the I lost the the slide
NOTE Confidence: 0.825598331142857

00:06:56.154 --> 00:06:59.368 about our major therapy today is
NOTE Confidence: 0.825598331142857

00:06:59.368 --> 00:07:02.308 is surgery and although getting
NOTE Confidence: 0.825598331142857

00:07:02.308 --> 00:07:05.708 children to a Kasai procedure is
NOTE Confidence: 0.825598331142857

00:07:05.708 --> 00:07:08.418 the the preferred treatment today,
NOTE Confidence: 0.825598331142857

00:07:08.420 --> 00:07:10.639 many of the hepatologists I spoke to
NOTE Confidence: 0.825598331142857

00:07:10.639 --> 00:07:12.764 wish that there were medical therapies
NOTE Confidence: 0.825598331142857

00:07:12.764 --> 00:07:14.990 that could help people either avoid
NOTE Confidence: 0.825598331142857

00:07:14.990 --> 00:07:17.255 or at least extend the time that.
NOTE Confidence: 0.825598331142857

00:07:17.260 --> 00:07:19.010 It would take to get to surgery.
NOTE Confidence: 0.69245006

00:07:21.900 --> 00:07:25.266 Other hepatologists that I spoke to.
NOTE Confidence: 0.69245006

00:07:25.270 --> 00:07:27.514 Saying different things that have really
NOTE Confidence: 0.69245006

00:07:27.514 --> 00:07:29.659 impacted their practice and they stated
NOTE Confidence: 0.69245006

00:07:29.659 --> 00:07:32.035 that this technology has has changed how I
NOTE Confidence: 0.69245006

00:07:32.090 --> 00:07:34.256 diagnosed and practiced hepatology today.

NOTE Confidence: 0.69245006

00:07:34.256 --> 00:07:36.624 Here's a picture of Bob Dylan from the

NOTE Confidence: 0.69245006

00:07:36.624 --> 00:07:38.726 1970s and you'll actually notice that a

NOTE Confidence: 0.69245006

00:07:38.726 --> 00:07:41.372 lot of our major categories for needle

NOTE Confidence: 0.69245006

00:07:41.372 --> 00:07:43.264 needle Cholestasis haven't changed.

NOTE Confidence: 0.69245006

00:07:43.270 --> 00:07:47.734 So about 1/4 of the patients that we see

NOTE Confidence: 0.69245006

00:07:47.734 --> 00:07:50.124 who have conjugated hyperbilirubinemia

NOTE Confidence: 0.69245006

00:07:50.124 --> 00:07:52.110 have biliary atresia,

NOTE Confidence: 0.69245006

00:07:52.110 --> 00:07:56.230 about 3 to 5% have a viral infection.

NOTE Confidence: 0.69245006

00:07:56.230 --> 00:07:57.304 Of some kind.

NOTE Confidence: 0.69245006

00:07:57.304 --> 00:08:01.234 But in the 1970s you know more than 2/3 of

NOTE Confidence: 0.69245006

00:08:01.234 --> 00:08:04.363 kids had what we termed neonatal hepatitis,

NOTE Confidence: 0.69245006

00:08:04.370 --> 00:08:07.457 which really is idiopathic, where you know,

NOTE Confidence: 0.69245006

00:08:07.460 --> 00:08:09.900 we just didn't know what the pathology was.

NOTE Confidence: 0.69245006

00:08:09.900 --> 00:08:12.119 Now it's time God has gone on.

NOTE Confidence: 0.69245006

00:08:12.120 --> 00:08:13.836 Obviously Bob Dylan's gotten a little

NOTE Confidence: 0.69245006

00:08:13.836 --> 00:08:17.104 bit older, wiser, more grizzled.
NOTE Confidence: 0.69245006

00:08:17.104 --> 00:08:20.696 We understand much better
NOTE Confidence: 0.69245006

00:08:20.696 --> 00:08:22.192 potential mechanisms.
NOTE Confidence: 0.69245006

00:08:22.192 --> 00:08:24.560 We we now understand.
NOTE Confidence: 0.69245006

00:08:24.560 --> 00:08:26.790 Things such as A1 antitrypsin.
NOTE Confidence: 0.69245006

00:08:26.790 --> 00:08:29.796 Disease, metabolic disease.
NOTE Confidence: 0.69245006

00:08:29.796 --> 00:08:33.804 Various metabolic causes of
NOTE Confidence: 0.69245006

00:08:33.804 --> 00:08:35.808 intrahepatic Cholestasis.
NOTE Confidence: 0.69245006

00:08:35.810 --> 00:08:37.765 There does remain a small
NOTE Confidence: 0.69245006

00:08:37.765 --> 00:08:39.275 proportion instead of 65%.
NOTE Confidence: 0.69245006

00:08:39.275 --> 00:08:42.510 Now about 10 to 15% of our patients,
NOTE Confidence: 0.69245006

00:08:42.510 --> 00:08:44.070 which remain undefined,
NOTE Confidence: 0.69245006

00:08:44.070 --> 00:08:47.094 but the technology that that these
NOTE Confidence: 0.69245006

00:08:47.094 --> 00:08:49.110 have ethologists were talking
NOTE Confidence: 0.69245006

00:08:49.198 --> 00:08:52.102 about have really changed how they
NOTE Confidence: 0.69245006

00:08:52.102 --> 00:08:53.838 practice their clinical hematology.

NOTE Confidence: 0.69245006

00:08:53.838 --> 00:08:58.078 Of course, the the most common.

NOTE Confidence: 0.69245006

00:08:58.080 --> 00:09:01.530 Cause of hyperbilirubinemia.

NOTE Confidence: 0.69245006

00:09:01.530 --> 00:09:04.827 In this age range remains biliary atresia.

NOTE Confidence: 0.69245006

00:09:04.830 --> 00:09:06.410 There was the discovery

NOTE Confidence: 0.69245006

00:09:06.410 --> 00:09:07.990 of A1 antitrypsin disease,

NOTE Confidence: 0.69245006

00:09:07.990 --> 00:09:11.714 and it can be quickly screened for.

NOTE Confidence: 0.69245006

00:09:11.720 --> 00:09:12.270 You know,

NOTE Confidence: 0.69245006

00:09:12.270 --> 00:09:14.470 and then there are a number of rare

NOTE Confidence: 0.69245006

00:09:14.536 --> 00:09:17.231 diseases which we can go through different

NOTE Confidence: 0.69245006

00:09:17.231 --> 00:09:19.800 kinds of biochemical or imaging modalities,

NOTE Confidence: 0.69245006

00:09:19.800 --> 00:09:23.167 but one which was not really available

NOTE Confidence: 0.69245006

00:09:23.167 --> 00:09:27.836 5 to 10 years ago because of cost is

NOTE Confidence: 0.69245006

00:09:27.836 --> 00:09:30.556 genotyping and whole genome sequencing.

NOTE Confidence: 0.69245006

00:09:30.560 --> 00:09:33.136 And you know that that really relates to

NOTE Confidence: 0.69245006

00:09:33.136 --> 00:09:35.818 how much sequencing the genome has had.

NOTE Confidence: 0.69245006

00:09:35.820 --> 00:09:38.116 The cost has followed where you know in
NOTE Confidence: 0.69245006

00:09:38.120 --> 00:09:39.919 2001 to to sequence of persons genome.
NOTE Confidence: 0.69245006

00:09:39.920 --> 00:09:41.768 It cost more than \$100 million.
NOTE Confidence: 0.69245006

00:09:41.770 --> 00:09:44.250 We're now at about 1000 or maybe under
NOTE Confidence: 0.69245006

00:09:44.250 --> 00:09:46.386 \$1000 to sequence a person's genome,
NOTE Confidence: 0.69245006

00:09:46.390 --> 00:09:49.540 so you know it's now become cost
NOTE Confidence: 0.69245006

00:09:49.540 --> 00:09:51.988 competitive to to quickly go and sequence,
NOTE Confidence: 0.69245006

00:09:51.990 --> 00:09:53.873 and it's actually the the the roadblock
NOTE Confidence: 0.69245006

00:09:53.873 --> 00:09:56.009 now is on the bioinformatic side.
NOTE Confidence: 0.69245006

00:09:56.010 --> 00:09:58.950 How quickly can we get the information
NOTE Confidence: 0.69245006

00:09:58.950 --> 00:10:02.364 back once we send persons DNA and
NOTE Confidence: 0.69245006

00:10:02.364 --> 00:10:05.262 it's really changed for a lot of
NOTE Confidence: 0.69245006

00:10:05.262 --> 00:10:07.467 hepatologists you know where we put
NOTE Confidence: 0.69245006

00:10:07.470 --> 00:10:09.970 genotyping or whole exome sequencing
NOTE Confidence: 0.69245006

00:10:09.970 --> 00:10:13.290 in the in the diagnostic criteria?
NOTE Confidence: 0.69245006

00:10:13.290 --> 00:10:15.306 Now the this is one of the.

NOTE Confidence: 0.69245006
00:10:15.310 --> 00:10:17.308 This is a neonatal Cholestasis panel.
NOTE Confidence: 0.69245006
00:10:17.310 --> 00:10:18.900 Actually this can be used on
NOTE Confidence: 0.69245006
00:10:18.900 --> 00:10:20.586 both children and and adults,
NOTE Confidence: 0.69245006
00:10:20.586 --> 00:10:23.594 and you can see I think there's 30
NOTE Confidence: 0.69245006
00:10:23.594 --> 00:10:26.408 something genes on this on this panel.
NOTE Confidence: 0.69245006
00:10:26.410 --> 00:10:28.858 If one quickly looks at the panel though,
NOTE Confidence: 0.69245006
00:10:28.860 --> 00:10:30.450 you know there's very few.
NOTE Confidence: 0.69245006
00:10:30.450 --> 00:10:30.866 I think.
NOTE Confidence: 0.69245006
00:10:30.866 --> 00:10:32.322 I'm sure I have missed a few,
NOTE Confidence: 0.69245006
00:10:32.330 --> 00:10:35.993 but the ones I've marked in red are genes
NOTE Confidence: 0.69245006
00:10:35.993 --> 00:10:39.888 that actually have a therapy for CFTR.
NOTE Confidence: 0.69245006
00:10:39.888 --> 00:10:43.260 We may have a a therapy.
NOTE Confidence: 0.69245006
00:10:43.260 --> 00:10:47.775 For the liver disease we're waiting on.
NOTE Confidence: 0.69245006
00:10:47.780 --> 00:10:49.610 If the the current medications
NOTE Confidence: 0.69245006
00:10:49.610 --> 00:10:51.440 that treat lung liver disease
NOTE Confidence: 0.69245006

00:10:51.510 --> 00:10:53.098 treat liver liver disease,
NOTE Confidence: 0.69245006

00:10:53.100 --> 00:10:54.576 but you can see that leaves,
NOTE Confidence: 0.69245006

00:10:54.580 --> 00:10:56.570 you know a significant number
NOTE Confidence: 0.69245006

00:10:56.570 --> 00:10:58.560 of genes where we actually
NOTE Confidence: 0.826571591875

00:10:58.635 --> 00:11:01.126 know the the the genetic defect but
NOTE Confidence: 0.826571591875

00:11:01.126 --> 00:11:02.556 don't have an effective therapy.
NOTE Confidence: 0.826571591875

00:11:02.560 --> 00:11:04.906 And as one hepatologist told me,
NOTE Confidence: 0.826571591875

00:11:04.910 --> 00:11:06.950 you know it's it's nice to be able
NOTE Confidence: 0.826571591875

00:11:06.950 --> 00:11:09.238 to tell people that you know their
NOTE Confidence: 0.826571591875

00:11:09.238 --> 00:11:11.660 child has a has a disease name,
NOTE Confidence: 0.826571591875

00:11:11.660 --> 00:11:13.250 even if there isn't current.
NOTE Confidence: 0.826571591875

00:11:13.250 --> 00:11:16.118 Therapy, but on the other hand,
NOTE Confidence: 0.826571591875

00:11:16.120 --> 00:11:18.241 you know it feels a little bit
NOTE Confidence: 0.826571591875

00:11:18.241 --> 00:11:20.667 that you know our job is just to
NOTE Confidence: 0.826571591875

00:11:20.667 --> 00:11:22.921 keep them as healthy as possible so
NOTE Confidence: 0.826571591875

00:11:22.921 --> 00:11:25.228 that they can get to a transplant.

NOTE Confidence: 0.826571591875

00:11:25.230 --> 00:11:27.024 Whether that means that they get

NOTE Confidence: 0.826571591875

00:11:27.024 --> 00:11:28.977 to the size of the transplant

NOTE Confidence: 0.826571591875

00:11:28.977 --> 00:11:32.162 or that they don't get too sick

NOTE Confidence: 0.826571591875

00:11:32.162 --> 00:11:35.910 before needing the transplant. Umm?

NOTE Confidence: 0.826571591875

00:11:35.910 --> 00:11:38.164 In my research though for this talk,

NOTE Confidence: 0.826571591875

00:11:38.170 --> 00:11:40.570 I saw that you know there are there.

NOTE Confidence: 0.826571591875

00:11:40.570 --> 00:11:42.754 There was actually a very recent

NOTE Confidence: 0.826571591875

00:11:42.754 --> 00:11:45.330 paper that came out where a group

NOTE Confidence: 0.826571591875

00:11:45.330 --> 00:11:47.430 at Beth Israel actually came up

NOTE Confidence: 0.826571591875

00:11:47.430 --> 00:11:49.810 with the synthetic form of ABC

NOTE Confidence: 0.826571591875

00:11:49.810 --> 00:11:52.362 before they treated actually a mouse

NOTE Confidence: 0.826571591875

00:11:52.362 --> 00:11:54.730 model of this deficiency.

NOTE Confidence: 0.826571591875

00:11:54.730 --> 00:11:56.788 But what I found you've actually

NOTE Confidence: 0.826571591875

00:11:56.788 --> 00:11:58.561 more interesting is actually the

NOTE Confidence: 0.826571591875

00:11:58.561 --> 00:12:00.589 company that that funded this therapy,

NOTE Confidence: 0.826571591875

00:12:00.590 --> 00:12:02.834 and obviously it's a company that
NOTE Confidence: 0.826571591875

00:12:02.834 --> 00:12:05.943 we're all familiar with in in 2022 now.
NOTE Confidence: 0.826571591875

00:12:05.943 --> 00:12:09.860 That's provided a number of, you know,
NOTE Confidence: 0.826571591875

00:12:09.860 --> 00:12:13.760 vaccines. So this company Moderna.
NOTE Confidence: 0.826571591875

00:12:13.760 --> 00:12:16.623 Is providing M RNA that can be
NOTE Confidence: 0.826571591875

00:12:16.623 --> 00:12:18.570 synthesized and targeted to that
NOTE Confidence: 0.826571591875

00:12:18.570 --> 00:12:20.810 aside so you know there is at
NOTE Confidence: 0.826571591875

00:12:20.810 --> 00:12:23.705 least a hope that we will be able
NOTE Confidence: 0.826571591875

00:12:23.705 --> 00:12:25.611 to develop therapies for a lot
NOTE Confidence: 0.826571591875

00:12:25.611 --> 00:12:26.719 of these monoallelic diseases,
NOTE Confidence: 0.826571591875

00:12:26.720 --> 00:12:29.400 but it obviously you know how do we
NOTE Confidence: 0.826571591875

00:12:29.400 --> 00:12:31.656 translate that to each of our patients
NOTE Confidence: 0.826571591875

00:12:31.656 --> 00:12:34.060 and and make it cost effective?
NOTE Confidence: 0.826571591875

00:12:34.060 --> 00:12:35.420 I think are still barriers.
NOTE Confidence: 0.826571591875

00:12:35.420 --> 00:12:37.212 And how do we get that through
NOTE Confidence: 0.826571591875

00:12:37.212 --> 00:12:37.724 regulatory approval?

NOTE Confidence: 0.90302501

00:12:39.240 --> 00:12:40.744 We're going to need to wrap up in

NOTE Confidence: 0.90302501

00:12:40.744 --> 00:12:42.409 about a minute or so if you can,

NOTE Confidence: 0.7720783985

00:12:42.450 --> 00:12:43.932 that's fine, so I'm just going

NOTE Confidence: 0.7720783985

00:12:43.932 --> 00:12:45.494 to run through this. Which is.

NOTE Confidence: 0.7720783985

00:12:45.494 --> 00:12:47.216 This is the biggest problem that

NOTE Confidence: 0.7720783985

00:12:47.216 --> 00:12:49.307 people see in the hepatology practice,

NOTE Confidence: 0.7720783985

00:12:49.310 --> 00:12:53.405 and the pun is really about mash.

NOTE Confidence: 0.7720783985

00:12:53.410 --> 00:12:55.400 It's clearly a growing problem,

NOTE Confidence: 0.7720783985

00:12:55.400 --> 00:12:57.060 you know, the question is,

NOTE Confidence: 0.7720783985

00:12:57.060 --> 00:12:59.916 what do we tell our patients?

NOTE Confidence: 0.7720783985

00:12:59.920 --> 00:13:05.260 We have very little data for for children.

NOTE Confidence: 0.7720783985

00:13:05.260 --> 00:13:08.060 Most of our insights come from adults.

NOTE Confidence: 0.7720783985

00:13:08.060 --> 00:13:09.290 I'm just going to show you.

NOTE Confidence: 0.7720783985

00:13:09.290 --> 00:13:10.645 Some data that we have

NOTE Confidence: 0.7720783985

00:13:10.645 --> 00:13:11.729 actually just worked on.

NOTE Confidence: 0.7720783985

00:13:11.730 --> 00:13:13.676 We looked at both adults as well
NOTE Confidence: 0.7720783985

00:13:13.676 --> 00:13:15.518 as a pediatric ward for adults.
NOTE Confidence: 0.7720783985

00:13:15.520 --> 00:13:17.488 When you look at the Histology,
NOTE Confidence: 0.7720783985

00:13:17.490 --> 00:13:18.790 you actually can predict
NOTE Confidence: 0.7720783985

00:13:18.790 --> 00:13:20.090 very well their fibrosis,
NOTE Confidence: 0.7720783985

00:13:20.090 --> 00:13:22.547 but that correlation does not hold up
NOTE Confidence: 0.7720783985

00:13:22.547 --> 00:13:25.389 in children and you know we need to
NOTE Confidence: 0.7720783985

00:13:25.389 --> 00:13:27.909 really build much larger cohorts and sample.
NOTE Confidence: 0.7720783985

00:13:27.910 --> 00:13:30.966 We think that the genes that are
NOTE Confidence: 0.7720783985

00:13:30.966 --> 00:13:33.894 some genes that are preserved in.
NOTE Confidence: 0.7720783985

00:13:33.900 --> 00:13:36.125 In both pediatric and adult
NOTE Confidence: 0.7720783985

00:13:36.125 --> 00:13:37.015 national preserve,
NOTE Confidence: 0.7720783985

00:13:37.020 --> 00:13:38.791 but there are many other genes which
NOTE Confidence: 0.7720783985

00:13:38.791 --> 00:13:40.319 just really have no correlation.
NOTE Confidence: 0.7720783985

00:13:40.320 --> 00:13:41.526 So you know,
NOTE Confidence: 0.7720783985

00:13:41.526 --> 00:13:43.536 just to summarize my work

NOTE Confidence: 0.7720783985

00:13:43.536 --> 00:13:45.878 and that of my colleagues.

NOTE Confidence: 0.7720783985

00:13:45.880 --> 00:13:46.516 You know,

NOTE Confidence: 0.7720783985

00:13:46.516 --> 00:13:48.424 for a lot of pediatric diseases

NOTE Confidence: 0.7720783985

00:13:48.424 --> 00:13:50.472 are our current modalities just

NOTE Confidence: 0.7720783985

00:13:50.472 --> 00:13:52.264 don't reflect the heterogeneous

NOTE Confidence: 0.7720783985

00:13:52.264 --> 00:13:54.389 causes and we don't have.

NOTE Confidence: 0.7720783985

00:13:54.390 --> 00:13:55.790 Because we don't know what

NOTE Confidence: 0.7720783985

00:13:55.790 --> 00:13:56.910 the specific causes are,

NOTE Confidence: 0.7720783985

00:13:56.910 --> 00:14:00.752 we have a hard time targeting therapy.

NOTE Confidence: 0.7720783985

00:14:00.752 --> 00:14:04.607 We know many monogenetic diseases,

NOTE Confidence: 0.7720783985

00:14:04.610 --> 00:14:08.726 but we don't have an effective strategy.

NOTE Confidence: 0.7720783985

00:14:08.730 --> 00:14:10.062 And finally,

NOTE Confidence: 0.7720783985

00:14:10.062 --> 00:14:14.058 a pediatric Nash is rapidly growing.

NOTE Confidence: 0.7720783985

00:14:14.060 --> 00:14:16.000 It may be we think,

NOTE Confidence: 0.7720783985

00:14:16.000 --> 00:14:17.176 at least in the pediatric community,

NOTE Confidence: 0.7720783985

00:14:17.180 --> 00:14:18.875 that the pace of fibrosis
NOTE Confidence: 0.7720783985

00:14:18.875 --> 00:14:21.120 actually may be the most severe,
NOTE Confidence: 0.7720783985

00:14:21.120 --> 00:14:22.635 because they're presenting
NOTE Confidence: 0.7720783985

00:14:22.635 --> 00:14:25.160 so early and you know,
NOTE Confidence: 0.7720783985

00:14:25.160 --> 00:14:27.302 one of my colleagues suggested that
NOTE Confidence: 0.7720783985

00:14:27.302 --> 00:14:29.918 we include some of the older adults,
NOTE Confidence: 0.7720783985

00:14:29.920 --> 00:14:31.500 older adolescents I should say,
NOTE Confidence: 0.7720783985

00:14:31.500 --> 00:14:33.360 and the adult Nash studies so
NOTE Confidence: 0.7720783985

00:14:33.360 --> 00:14:34.980 that we can translate some
NOTE Confidence: 0.7720783985

00:14:34.980 --> 00:14:36.876 of these therapies to our our
NOTE Confidence: 0.7720783985

00:14:36.876 --> 00:14:38.620 patients a little bit quicker.
NOTE Confidence: 0.7720783985

00:14:38.620 --> 00:14:40.696 So thanks to all the people
NOTE Confidence: 0.7720783985

00:14:40.696 --> 00:14:42.889 who who gave me input so.
NOTE Confidence: 0.65049933

00:14:46.030 --> 00:14:48.860 That's not sure how. Thank you.