WEBVTT

NOTE duration:"01:00:42.2400000"

NOTE recognizability:0.826

NOTE language:en-us

NOTE Confidence: 0.757621294166667

00:00:00.000 --> 00:00:02.982 Everybody or we are very fortunate

NOTE Confidence: 0.757621294166667

 $00:00:02.982 \rightarrow 00:00:06.240$ today to have doctor Haluska here.

NOTE Confidence: 0.757621294166667

00:00:06.240 --> 00:00:09.672 Doctor Haluska is professor of John

NOTE Confidence: 0.757621294166667

00:00:09.672 --> 00:00:12.757 Hopkins and current chairman of

NOTE Confidence: 0.757621294166667

00:00:12.757 --> 00:00:15.549 Society of Cardiovascular Pathology.

NOTE Confidence: 0.757621294166667

00:00:15.550 --> 00:00:16.750 So I look at his CV,

NOTE Confidence: 0.757621294166667

00:00:16.750 --> 00:00:17.926 I look at that, my God,

NOTE Confidence: 0.757621294166667

00:00:17.930 --> 00:00:20.874 it's it's a really good example of

NOTE Confidence: 0.757621294166667

 $00:00:20.874 \longrightarrow 00:00:23.598$ academic pathologist can read that he

NOTE Confidence: 0.757621294166667

00:00:23.598 --> 00:00:26.566 graduated from Big Forest and did his

NOTE Confidence: 0.757621294166667

 $00{:}00{:}26.566$ --> $00{:}00{:}29.906$ AP and Fellowship at Johns Hopkins.

NOTE Confidence: 0.757621294166667

 $00{:}00{:}29{.}910 \dashrightarrow 00{:}00{:}31{.}122$ For the diagnostic part,

NOTE Confidence: 0.757621294166667

 $00:00:31.122 \longrightarrow 00:00:33.811$ I think a lot of people have joined

 $00:00:33.811 \rightarrow 00:00:36.223$ this diagnostic meeting in the morning,

NOTE Confidence: 0.757621294166667

 $00:00:36.230 \rightarrow 00:00:39.280$ right is internationally well known

NOTE Confidence: 0.757621294166667

00:00:39.280 --> 00:00:41.720 cardiovascular pathologist not only

NOTE Confidence: 0.757621294166667

00:00:41.720 --> 00:00:45.110 practice in John Hopkins but also have

NOTE Confidence: 0.757621294166667

 $00{:}00{:}45.110 \dashrightarrow 00{:}00{:}47.336$ consulting service from local hospital

NOTE Confidence: 0.757621294166667

 $00:00:47.336 \dashrightarrow 00:00:51.390$ and also as far as from Texas, Texas.

NOTE Confidence: 0.757621294166667

 $00:00:51.390 \longrightarrow 00:00:54.174$ So as the investigator,

NOTE Confidence: 0.757621294166667

00:00:54.174 --> 00:00:59.008 he published 220 publications including

NOTE Confidence: 0.8352534275

 $00{:}00{:}59{.}530 \dashrightarrow 00{:}01{:}01{.}558$ reviews and Case report

NOTE Confidence: 0.806599880833333

 $00:01:01.910 \longrightarrow 00:01:05.144$ and he is an internationally well

NOTE Confidence: 0.806599880833333

00:01:05.144 --> 00:01:08.310 known investigator for my micro RNA,

NOTE Confidence: 0.806599880833333

 $00:01:08.310 \rightarrow 00:01:12.830$ especially related to cardiovascular disease.

NOTE Confidence: 0.806599880833333

 $00:01:12.830 \rightarrow 00:01:17.186$ His current research are supported by two

NOTE Confidence: 0.806599880833333

 $00:01:17.190 \dashrightarrow 00:01:22.486$ R1SP I and three Co investigator R1 Grant.

NOTE Confidence: 0.806599880833333

 $00:01:22.490 \longrightarrow 00:01:25.745$ As at the educator, the the course

NOTE Confidence: 0.806599880833333

 $00:01:25.745 \longrightarrow 00:01:28.610$ director for the medical school,

- NOTE Confidence: 0.806599880833333
- 00:01:28.610 --> 00:01:31.842 cost director for postgraduate,
- NOTE Confidence: 0.806599880833333
- $00:01:31.842 \longrightarrow 00:01:34.266$ Fellows and resident.
- NOTE Confidence: 0.806599880833333
- $00:01:34.270 \rightarrow 00:01:37.680$ Anymore too much.
- NOTE Confidence: 0.806599880833333
- $00{:}01{:}37.680 \dashrightarrow 00{:}01{:}41.795$ He is the he had the frequently speaker
- NOTE Confidence: 0.806599880833333
- $00:01:41.795 \longrightarrow 00:01:44.660$ at national and international meetings
- NOTE Confidence: 0.806599880833333
- 00:01:44.746 --> 00:01:48.507 and organize several sessions in the USAP.
- NOTE Confidence: 0.806599880833333
- $00:01:48.507 \rightarrow 00:01:54.323$ And one thing he mentored about 40 trainees.
- NOTE Confidence: 0.806599880833333
- $00:01:54.330 \rightarrow 00:01:55.790$ Couple of them already showed
- NOTE Confidence: 0.806599880833333
- 00:01:55.790 --> 00:01:59.128 their professor John Hopkins now.
- NOTE Confidence: 0.806599880833333
- $00:01:59.130 \dashrightarrow 00:02:02.203$ One thing I think not very classical
- NOTE Confidence: 0.806599880833333
- $00:02:02.203 \rightarrow 00:02:04.550$ typical of academic pathologist,
- NOTE Confidence: 0.806599880833333
- $00{:}02{:}04.550 \dashrightarrow 00{:}02{:}07.693$ he has a full patent and invention
- NOTE Confidence: 0.806599880833333
- $00:02:07.693 \longrightarrow 00:02:10.858$ and he still have the potential
- NOTE Confidence: 0.7388189675
- $00{:}02{:}10.870 \dashrightarrow 00{:}02{:}15.170$ to be building there. Yeah. Thank you.
- NOTE Confidence: 0.880635388181818
- 00:02:15.760 --> 00:02:17.124 Thank you, Peter. Well,
- NOTE Confidence: 0.880635388181818

 $00:02:17.124 \rightarrow 00:02:19.420$ thank you very much for inviting me.

NOTE Confidence: 0.880635388181818

 $00:02:19.420 \longrightarrow 00:02:20.860$ Only 1/4 of what Peter

NOTE Confidence: 0.880635388181818

00:02:20.860 - 00:02:22.300 said about me was right.

NOTE Confidence: 0.880635388181818

00:02:22.300 --> 00:02:23.458 I won't tell you which quarter,

NOTE Confidence: 0.880635388181818

 $00:02:23.460 \longrightarrow 00:02:26.420$ but not the impressive stuff I'm certain of.

NOTE Confidence: 0.880635388181818

 $00:02:26.420 \dashrightarrow 00:02:29.220$ It is an absolute pleasure to be here.

NOTE Confidence: 0.880635388181818

 $00{:}02{:}29{.}220 \dashrightarrow 00{:}02{:}32{.}889$ At Yale, yes.

NOTE Confidence: 0.880635388181818

 $00:02:32.890 \longrightarrow 00:02:34.530$ I do not know how to turn the chime off.

NOTE Confidence: 0.647799262

00:02:35.330 --> 00:02:39.310 Do you know? Currently, apparently.

NOTE Confidence: 0.706623653333333

00:02:39.580 --> 00:02:41.596 OK, I don't wanna disrupt anything.

NOTE Confidence: 0.749212409

 $00:02:45.930 \longrightarrow 00:02:47.120$ And I'm sure that's the sound of

NOTE Confidence: 0.749212409

 $00:02:47.120 \longrightarrow 00:02:48.353$ people coming on, which is fine.

NOTE Confidence: 0.749212409

00:02:48.353 --> 00:02:49.799 I I will know sort of.

NOTE Confidence: 0.749212409

 $00:02:49.800 \longrightarrow 00:02:51.303$ At my wedding we had a video at the

NOTE Confidence: 0.749212409

 $00{:}02{:}51{.}303 \dashrightarrow 00{:}02{:}52{.}896$ end and I saw a guy walking on the

NOTE Confidence: 0.749212409

 $00{:}02{:}52{.}896 \dashrightarrow 00{:}02{:}54{.}543$ video and the last two minutes of the

- NOTE Confidence: 0.749212409
- $00:02:54.543 \rightarrow 00:02:56.136$ wedding he missed the whole thing,

 $00:02:56.136 \longrightarrow 00:02:58.747$ but we we documented that he showed

NOTE Confidence: 0.749212409

 $00:02:58.747 \rightarrow 00:03:01.598$ up late and our wedding started on

NOTE Confidence: 0.749212409

 $00:03:01.598 \rightarrow 00:03:03.640$ time just like today, which is great.

NOTE Confidence: 0.861866645555556

 $00:03:05.970 \dashrightarrow 00:03:07.986$ I I don't know if you're gonna find that.

NOTE Confidence: 0.881450133333333

 $00:03:11.350 \longrightarrow 00:03:13.066$ It's not going to bother me.

NOTE Confidence: 0.881450133333333

00:03:13.070 - 00:03:15.700 Then you can bring up.

NOTE Confidence: 0.881450133333333

00:03:15.700 --> 00:03:16.960 Yes, Sir, I'm. That's where I am.

NOTE Confidence: 0.65727773

00:03:18.500 --> 00:03:24.820 This, yeah. Adopted. It's not here yet.

NOTE Confidence: 0.7465352725

 $00:03:26.910 \longrightarrow 00:03:27.930$ Nope, doesn't give me

NOTE Confidence: 0.809751363333333

 $00:03:27.940 \longrightarrow 00:03:29.732$ that option. That's where

NOTE Confidence: 0.809751363333333

00:03:29.732 --> 00:03:31.299 I am. Very long time.

NOTE Confidence: 0.015140802

00:03:36.710 --> 00:03:37.730 Recipients.

NOTE Confidence: 0.884970118

 $00:03:49.490 \rightarrow 00:03:51.614$ I think now everybody has, everyone has

NOTE Confidence: 0.884970118

 $00:03:51.614 \dashrightarrow 00:03:53.550$ used these extra few minutes to join us.

 $00:03:53.550 \longrightarrow 00:03:55.290$ I don't think we'll be hearing

NOTE Confidence: 0.884970118

 $00{:}03{:}55{.}290 \dashrightarrow 00{:}03{:}56{.}450$ the ringing much more.

NOTE Confidence: 0.884970118

 $00{:}03{:}56{.}450 \dashrightarrow 00{:}03{:}58{.}277$ So I want to again thank you so much

NOTE Confidence: 0.884970118

 $00:03:58.277 \rightarrow 00:04:00.267$ for inviting me to come to Yale today.

NOTE Confidence: 0.884970118

 $00:04:00.270 \dashrightarrow 00:04:02.646$ It is an absolute pleasure to be here.

NOTE Confidence: 0.884970118

 $00:04:02.650 \rightarrow 00:04:05.188$ For those of you who are watching as well,

NOTE Confidence: 0.884970118

00:04:05.190 --> 00:04:07.080 it's nice to see you all remotely.

NOTE Confidence: 0.884970118

00:04:07.080 --> 00:04:09.678 I'm going to be talking about

NOTE Confidence: 0.884970118

00:04:09.678 --> 00:04:10.977 diagnosing myocarditis challenges.

NOTE Confidence: 0.884970118

 $00{:}04{:}10{.}980 \dashrightarrow 00{:}04{:}13{.}600$ And opportunities.

NOTE Confidence: 0.884970118

00:04:13.600 --> 00:04:16.218 Should I get this to move forward?

NOTE Confidence: 0.884970118

00:04:16.220 --> 00:04:17.088 And I should say,

NOTE Confidence: 0.884970118

 $00:04:17.088 \longrightarrow 00:04:18.710$ for the first time in my life,

NOTE Confidence: 0.884970118

 $00{:}04{:}18.710 \dashrightarrow 00{:}04{:}20.170$ I actually have a disclosure.

NOTE Confidence: 0.884970118

 $00:04:20.170 \longrightarrow 00:04:22.368$ I just started consulting for a company.

NOTE Confidence: 0.884970118

 $00:04:22.370 \rightarrow 00:04:23.528$ I haven't gotten a dime yet,

 $00{:}04{:}23.530 \dashrightarrow 00{:}04{:}25.570$ but I'm awfully excited about the

NOTE Confidence: 0.884970118

 $00:04:25.570 \rightarrow 00:04:27.484$ possibility of that happening and I

NOTE Confidence: 0.884970118

 $00{:}04{:}27{.}484 \dashrightarrow 00{:}04{:}29{.}206$ needed to share that with you here.

NOTE Confidence: 0.884970118

 $00:04:29.210 \longrightarrow 00:04:30.788$ So I have a few objectives.

NOTE Confidence: 0.884970118

 $00{:}04{:}30.790 \dashrightarrow 00{:}04{:}32.986$ They are to recognize the challenges

NOTE Confidence: 0.884970118

 $00{:}04{:}32{.}986 \dashrightarrow 00{:}04{:}35{.}130$ in making a myocarditis diagnosis,

NOTE Confidence: 0.884970118

 $00{:}04{:}35{.}130 \dashrightarrow 00{:}04{:}37{.}050$ explain why that challenge causes

NOTE Confidence: 0.884970118

 $00:04:37.050 \rightarrow 00:04:38.970$ difficulties in the general population,

NOTE Confidence: 0.884970118

 $00{:}04{:}38{.}970 \dashrightarrow 00{:}04{:}41{.}388$ and learn about new directions to

NOTE Confidence: 0.884970118

 $00:04:41.388 \longrightarrow 00:04:43.000$ improve the myocarditis diagnosis

NOTE Confidence: 0.884970118

 $00:04:43.065 \longrightarrow 00:04:44.509$ that we are undertaking.

NOTE Confidence: 0.884970118

 $00{:}04{:}44{.}510 \dashrightarrow 00{:}04{:}45{.}658$ And this is what I'm going to

NOTE Confidence: 0.884970118

 $00{:}04{:}45.658 \dashrightarrow 00{:}04{:}46.470$ try and talk to you.

NOTE Confidence: 0.884970118

00:04:46.470 --> 00:04:47.040 About today,

NOTE Confidence: 0.884970118

 $00{:}04{:}47{.}040 \dashrightarrow 00{:}04{:}49{.}035$ I'll keep coming back to this slide,

 $00:04:49.040 \rightarrow 00:04:50.504$ which is of course I want to give

NOTE Confidence: 0.884970118

 $00:04:50.504 \longrightarrow 00:04:52.138$ you a little bit of information

NOTE Confidence: 0.884970118

 $00:04:52.138 \longrightarrow 00:04:53.358$ about what is myocarditis.

NOTE Confidence: 0.884970118

 $00{:}04{:}53{.}360 \dashrightarrow 00{:}04{:}55{.}390$ Then talk about different ways

NOTE Confidence: 0.884970118

 $00:04:55.390 \longrightarrow 00:04:57.014$ that myocarditis is diagnosed.

NOTE Confidence: 0.884970118

 $00{:}04{:}57{.}020 \dashrightarrow 00{:}04{:}58{.}495$ Spend some time talking about

NOTE Confidence: 0.884970118

 $00:04:58.495 \longrightarrow 00:04:59.380$ the Dallas criteria,

NOTE Confidence: 0.884970118

 $00:04:59.380 \longrightarrow 00:05:02.124$ which is what we use in Histology and

NOTE Confidence: 0.884970118

 $00{:}05{:}02{.}124 \dashrightarrow 00{:}05{:}05{.}196$ then our our attempts to revise the

NOTE Confidence: 0.884970118

 $00{:}05{:}05{.}196$ --> $00{:}05{:}07{.}506$ Dallas criteria and then diagnosing

NOTE Confidence: 0.884970118

 $00:05:07.585 \rightarrow 00:05:10.270$ myocarditis beyond the immune cells.

NOTE Confidence: 0.884970118

 $00:05:10.270 \dashrightarrow 00:05:12.442$ So let's start with a straightforward

NOTE Confidence: 0.884970118

 $00:05:12.442 \longrightarrow 00:05:13.528$ definition of myocarditis.

NOTE Confidence: 0.884970118

 $00:05:13.530 \longrightarrow 00:05:15.220$ This is inflammation of the

NOTE Confidence: 0.884970118

 $00{:}05{:}15{.}220 \dashrightarrow 00{:}05{:}16{.}572$ heart with myocyte in jury.

NOTE Confidence: 0.884970118

 $00:05:16.580 \rightarrow 00:05:18.603$ And we have a couple of Histology

- NOTE Confidence: 0.884970118
- $00:05:18.603 \rightarrow 00:05:20.302$ slides showing this classic pattern
- NOTE Confidence: 0.884970118
- $00:05:20.302 \longrightarrow 00:05:22.247$ of a inflammatory cell infiltrate.
- NOTE Confidence: 0.884970118
- $00{:}05{:}22{.}250 \dashrightarrow 00{:}05{:}24{.}343$ This happens to be a number of
- NOTE Confidence: 0.884970118
- $00:05:24.343 \rightarrow 00:05:26.190$ lymphocytes and some myocyte injury,
- NOTE Confidence: 0.884970118
- $00{:}05{:}26.190 \dashrightarrow 00{:}05{:}28.654$ both at a lower power and a
- NOTE Confidence: 0.884970118
- $00:05:28.654 \rightarrow 00:05:30.364$ higher power showing a number
- NOTE Confidence: 0.884970118
- $00:05:30.364 \rightarrow 00:05:31.820$ of these infiltrating cells.
- NOTE Confidence: 0.884970118
- $00:05:31.820 \rightarrow 00:05:34.046$ So that's a very straightforward definition.
- NOTE Confidence: 0.884970118
- $00:05:34.050 \rightarrow 00:05:36.842$ There are a number of causes of myocarditis
- NOTE Confidence: 0.884970118
- $00:05:36.842 \rightarrow 00:05:39.188$ that some of these are infectious.
- NOTE Confidence: 0.884970118
- $00:05:39.190 \rightarrow 00:05:41.318$ We have a number of different viruses.
- NOTE Confidence: 0.884970118
- $00:05:41.320 \rightarrow 00:05:44.180$ That are associated with myocarditis,
- NOTE Confidence: 0.884970118
- $00:05:44.180 \longrightarrow 00:05:45.392$ viral myocarditis and that's
- NOTE Confidence: 0.884970118
- $00:05:45.392 \rightarrow 00:05:47.580$ something we can test for by PCR
- NOTE Confidence: 0.884970118
- $00{:}05{:}47.580 \dashrightarrow 00{:}05{:}48.836$ sometimes identify what these
- NOTE Confidence: 0.884970118

 $00:05:48.836 \rightarrow 00:05:51.127$ viruses are and type them a number

NOTE Confidence: 0.884970118

 $00{:}05{:}51{.}127 \dashrightarrow 00{:}05{:}52{.}797$ of parasites can cause myocarditis.

NOTE Confidence: 0.884970118

00:05:52.800 --> 00:05:54.473 I brought up Lyme disease because I

NOTE Confidence: 0.884970118

 $00{:}05{:}54{.}473 \dashrightarrow 00{:}05{:}56{.}126$ am here excited to be in Connecticut

NOTE Confidence: 0.884970118

 $00{:}05{:}56{.}126 \dashrightarrow 00{:}05{:}57{.}014$ to give the talk.

NOTE Confidence: 0.884970118

 $00:05:57.020 \dashrightarrow 00:05:59.259$ So I had to bring that up as a big one.

NOTE Confidence: 0.884970118

 $00{:}05{:}59{.}260 \dashrightarrow 00{:}06{:}01{.}703$ But Chagas disease is a really big

NOTE Confidence: 0.884970118

 $00{:}06{:}01.703 \dashrightarrow 00{:}06{:}03.854$ problem in Central and South America

NOTE Confidence: 0.884970118

 $00{:}06{:}03.854 \dashrightarrow 00{:}06{:}06.255$ as a cause of myocarditis and then

NOTE Confidence: 0.884970118

 $00:06:06.323 \rightarrow 00:06:08.537$ we can also rarely see bacterial

NOTE Confidence: 0.884970118

00:06:08.537 --> 00:06:10.397 forms of myocarditis as well.

NOTE Confidence: 0.884970118

 $00{:}06{:}10.397 \dashrightarrow 00{:}06{:}13.036$ There's also a number of non infectious.

NOTE Confidence: 0.884970118

00:06:13.040 --> 00:06:14.423 Forms of myocarditis,

NOTE Confidence: 0.884970118

00:06:14.423 --> 00:06:16.728 autoimmune diseases such as lupus,

NOTE Confidence: 0.884970118

 $00{:}06{:}16.730 \dashrightarrow 00{:}06{:}18.765$ treatment related processes such as

NOTE Confidence: 0.884970118

00:06:18.765 --> 00:06:20.800 immune checkpoint and inhibitor myocarditis,

- NOTE Confidence: 0.884970118
- $00:06:20.800 \longrightarrow 00:06:22.680$ something which didn't exist 10

00:06:22.680 --> 00:06:24.184 or 15 years ago,

NOTE Confidence: 0.884970118

 $00:06:24.190 \longrightarrow 00:06:26.350$ antipsychotic agents and then

NOTE Confidence: 0.884970118

 $00:06:26.350 \longrightarrow 00:06:27.970$ even post vaccinations.

NOTE Confidence: 0.884970118

 $00{:}06{:}27{.}970 \dashrightarrow 00{:}06{:}29{.}965$ So there has been some reports which

NOTE Confidence: 0.884970118

00:06:29.965 --> 00:06:32.001 I think percentage of which are real

NOTE Confidence: 0.884970118

 $00:06:32.001 \rightarrow 00:06:34.000$ that there are associations with the SARS,

NOTE Confidence: 0.884970118

 $00{:}06{:}34.000 \dashrightarrow 00{:}06{:}36.280$ Kobe 2 vaccines and some

NOTE Confidence: 0.884970118

 $00{:}06{:}36{.}280 \dashrightarrow 00{:}06{:}38{.}560$ other vaccines that have been

NOTE Confidence: 0.926939567857143

 $00:06:38.646 \rightarrow 00:06:40.418$ reported in the past.

NOTE Confidence: 0.926939567857143

 $00:06:40.420 \rightarrow 00:06:42.484$ There are also many different subtypes

NOTE Confidence: 0.926939567857143

 $00{:}06{:}42{.}484 \dashrightarrow 00{:}06{:}44{.}473$ of myocarditis and this is again

NOTE Confidence: 0.926939567857143

 $00:06:44.473 \longrightarrow 00:06:46.135$ from a Histology point of view.

NOTE Confidence: 0.926939567857143

 $00{:}06{:}46{.}140 \dashrightarrow 00{:}06{:}48{.}744$ We have what I call our garden

NOTE Confidence: 0.926939567857143

00:06:48.744 --> 00:06:49.860 variety lymphocytic myocarditis,

 $00:06:49.860 \rightarrow 00:06:52.500$ lots of lymphocytes and myocyte damage.

NOTE Confidence: 0.926939567857143

 $00{:}06{:}52{.}500 \dashrightarrow 00{:}06{:}54{.}840$ We have giant cell myocarditis,

NOTE Confidence: 0.926939567857143

00:06:54.840 --> 00:06:57.630 a very specific entity of myocarditis,

NOTE Confidence: 0.926939567857143

 $00:06:57.630 \longrightarrow 00:06:59.736$ notable by the presence of these

NOTE Confidence: 0.926939567857143

 $00{:}06{:}59{.}736 \dashrightarrow 00{:}07{:}02{.}680$ large giant cells in the mix and a

NOTE Confidence: 0.926939567857143

 $00:07:02.680 \dashrightarrow 00:07:04.520$ very aggressive form of myocarditis.

NOTE Confidence: 0.926939567857143

 $00{:}07{:}04.520 \dashrightarrow 00{:}07{:}07{.}220$ And we can even have eosinophilic

NOTE Confidence: 0.926939567857143

 $00{:}07{:}07{.}220 \dashrightarrow 00{:}07{:}09{.}020$ myocarditis with numerous eosinophils

NOTE Confidence: 0.926939567857143

 $00{:}07{:}09{.}092 \dashrightarrow 00{:}07{:}10.868$ infiltrating from a variety.

NOTE Confidence: 0.926939567857143

 $00:07:10.870 \longrightarrow 00:07:15.178$ Processes one other.

NOTE Confidence: 0.926939567857143

 $00:07:15.180 \longrightarrow 00:07:16.564$ Type that gets lamped,

NOTE Confidence: 0.926939567857143

 $00:07:16.564 \longrightarrow 00:07:18.294$ lumped in with the other

NOTE Confidence: 0.926939567857143

00:07:18.294 --> 00:07:19.939 myocarditis forms is sarcoidosis,

NOTE Confidence: 0.926939567857143

 $00{:}07{:}19{.}940 \dashrightarrow 00{:}07{:}21{.}440$ which is considered a

NOTE Confidence: 0.926939567857143

 $00:07:21.440 \dashrightarrow 00:07:22.190$ granulomatous myocarditis.

NOTE Confidence: 0.926939567857143

00:07:22.190 --> 00:07:23.618 Some people might distinguish

- NOTE Confidence: 0.926939567857143
- $00:07:23.618 \rightarrow 00:07:25.760$ sarcoid as being a different process
- NOTE Confidence: 0.926939567857143
- $00:07:25.816 \rightarrow 00:07:27.706$ because it affects the entire body.
- NOTE Confidence: 0.926939567857143
- $00:07:27.710 \dashrightarrow 00:07:30.559$ A lot of people in the myocarditis
- NOTE Confidence: 0.926939567857143
- $00:07:30.559 \dashrightarrow 00:07:34.130$ world put it in as part of the process.
- NOTE Confidence: 0.926939567857143
- $00{:}07{:}34.130 \dashrightarrow 00{:}07{:}36.326$ There are a number of clinical
- NOTE Confidence: 0.926939567857143
- $00:07:36.326 \dashrightarrow 00:07:38.289$ features of myocarditis that we see,
- NOTE Confidence: 0.926939567857143
- $00:07:38.290 \longrightarrow 00:07:39.674$ a big one being chest pain and I
- NOTE Confidence: 0.926939567857143
- $00:07:39.674 \dashrightarrow 00:07:41.067$ stole this picture off the Internet.
- NOTE Confidence: 0.926939567857143
- $00:07:41.070 \dashrightarrow 00:07:43.886$ I just thought it was a good example.
- NOTE Confidence: 0.926939567857143
- 00:07:43.890 --> 00:07:46.258 New onset heart failure,
- NOTE Confidence: 0.926939567857143
- 00:07:46.258 --> 00:07:48.626 arrhythmias and conduction disturbances,
- NOTE Confidence: 0.926939567857143
- 00:07:48.630 --> 00:07:49.971 hemodynamic compromise and
- NOTE Confidence: 0.926939567857143
- $00:07:49.971 \dashrightarrow 00:07:51.759$ unfortunately debt where there's
- NOTE Confidence: 0.926939567857143
- $00:07:51.759 \longrightarrow 00:07:54.392$ a report of over 40,000 yearly
- NOTE Confidence: 0.926939567857143
- $00{:}07{:}54.392 \dashrightarrow 00{:}07{:}56.437$ deaths from forms of myocarditis.
- NOTE Confidence: 0.926939567857143

00:07:56.440 --> 00:07:57.854 A lot of that is Chagas disease,

NOTE Confidence: 0.926939567857143

 $00:07:57.860 \longrightarrow 00:08:00.188$ sort of chronic processes from that,

NOTE Confidence: 0.926939567857143

00:08:00.190 --> 00:08:00.946 but it also,

NOTE Confidence: 0.926939567857143

 $00:08:00.946 \longrightarrow 00:08:02.458$ we see this as viral myocarditis

NOTE Confidence: 0.926939567857143

 $00:08:02.458 \longrightarrow 00:08:03.817$ here in the United States.

NOTE Confidence: 0.926939567857143

 $00:08:03.820 \rightarrow 00:08:05.112$ Which unfortunately takes some

NOTE Confidence: 0.926939567857143

 $00:08:05.112 \longrightarrow 00:08:06.727$ number of lives every year.

NOTE Confidence: 0.85854478944444

 $00:08:09.160 \rightarrow 00:08:11.722$ So let's spend a little time talking

NOTE Confidence: 0.85854478944444

 $00{:}08{:}11.722 \dashrightarrow 00{:}08{:}13.658$ about how myocarditis is diagnosed

NOTE Confidence: 0.85854478944444

 $00:08:13.658 \rightarrow 00:08:15.974$ and we have biopsy based approaches,

NOTE Confidence: 0.85854478944444

 $00:08:15.980 \dashrightarrow 00:08:18.272$ imaging based approaches and

NOTE Confidence: 0.85854478944444

 $00:08:18.272 \rightarrow 00:08:21.137$ clinically based approaches as well.

NOTE Confidence: 0.85854478944444

 $00{:}08{:}21.140 \dashrightarrow 00{:}08{:}22.965$ And let's start with the

NOTE Confidence: 0.85854478944444

00:08:22.965 --> 00:08:23.695 endomyocardial biopsy.

NOTE Confidence: 0.85854478944444

 $00{:}08{:}23.700 \dashrightarrow 00{:}08{:}25.120$ So endomy ocardial biopsies are

NOTE Confidence: 0.85854478944444

 $00{:}08{:}25{.}120 \dashrightarrow 00{:}08{:}27{.}250$ performed here with the caves bioptome

- NOTE Confidence: 0.85854478944444
- 00:08:27.305 00:08:28.850 where they take this bioptome,
- NOTE Confidence: 0.85854478944444
- $00:08:28.850 \rightarrow 00:08:31.636$ they go through the internal jugular vein,
- NOTE Confidence: 0.85854478944444
- $00:08:31.640 \longrightarrow 00:08:33.768$ go into the right side of the heart
- NOTE Confidence: 0.85854478944444
- $00:08:33.768 \longrightarrow 00:08:35.760$ onto the septum and with little
- NOTE Confidence: 0.85854478944444
- $00{:}08{:}35.760 \dashrightarrow 00{:}08{:}37.510$ pinchers they grab little pieces
- NOTE Confidence: 0.85854478944444
- 00:08:37.510 --> 00:08:39.796 of myocardium that look like this.
- NOTE Confidence: 0.85854478944444
- 00:08:39.800 --> 00:08:40.772 They pull it out,
- NOTE Confidence: 0.85854478944444
- $00:08:40.772 \rightarrow 00:08:43.510$ they give it to us and we make a diagnosis.
- NOTE Confidence: 0.85854478944444
- 00:08:43.510 --> 00:08:45.250 Typically we see from three
- NOTE Confidence: 0.85854478944444
- 00:08:45.250 --> 00:08:46.990 to five pieces of myocardium,
- NOTE Confidence: 0.85854478944444
- $00:08:46.990 \longrightarrow 00:08:48.445$ these small pieces from which
- NOTE Confidence: 0.85854478944444
- $00{:}08{:}48.445 \dashrightarrow 00{:}08{:}50.510$ we're asked to make the diagnosis.
- NOTE Confidence: 0.85854478944444
- $00:08:50.510 \dashrightarrow 00:08:53.009$ And then in the setting of myocarditis,
- NOTE Confidence: 0.85854478944444
- $00{:}08{:}53{.}010 \dashrightarrow 00{:}08{:}55{.}250$ we're looking for inflammatory cell
- NOTE Confidence: 0.85854478944444
- $00:08:55.250 \dashrightarrow 00:08:57.042$ infiltrates and myocyte damage.
- NOTE Confidence: 0.85854478944444

00:08:57.050 --> 00:08:59.545 I've highlighted with a CD3A

NOTE Confidence: 0.85854478944444

 $00{:}08{:}59{.}545 \dashrightarrow 00{:}09{:}02{.}210$ number of lymphocytes and with a

NOTE Confidence: 0.85854478944444

 $00:09:02.210 \longrightarrow 00:09:04.550$ C68A number of macrophages here.

NOTE Confidence: 0.85854478944444

 $00:09:04.550 \longrightarrow 00:09:07.544$ And we base this diagnosis of

NOTE Confidence: 0.85854478944444

 $00:09:07.544 \dashrightarrow 00:09:10.450$ myocarditis on the Dallas criteria.

NOTE Confidence: 0.85854478944444

 $00:09:10.450 \longrightarrow 00:09:12.394$ Which I'm going to spend some

NOTE Confidence: 0.85854478944444

 $00:09:12.394 \rightarrow 00:09:14.308$ more time talking about in a bit.

NOTE Confidence: 0.85854478944444

 $00:09:14.310 \rightarrow 00:09:17.126$ I think this was a very useful paper

NOTE Confidence: 0.85854478944444

00:09:17.126 --> 00:09:19.502 that came out for clinicians which

NOTE Confidence: 0.85854478944444

 $00{:}09{:}19{.}502 \dashrightarrow 00{:}09{:}22{.}037$ was the when to biopsy guidelines

NOTE Confidence: 0.85854478944444

 $00{:}09{:}22.037 \dashrightarrow 00{:}09{:}24.470$ from 2007 and it has, I don't know,

NOTE Confidence: 0.85854478944444

 $00:09:24.470 \longrightarrow 00:09:26.017$ I think you can see that OK,

NOTE Confidence: 0.85854478944444

 $00{:}09{:}26.020 \dashrightarrow 00{:}09{:}27.310$ but I'll I'll talk through it.

NOTE Confidence: 0.85854478944444

00:09:27.310 --> 00:09:29.188 It's a number of different clinical

NOTE Confidence: 0.85854478944444

 $00:09:29.188 \longrightarrow 00:09:30.727$ scenarios which are either good

NOTE Confidence: 0.85854478944444

 $00:09:30.727 \longrightarrow 00:09:32.149$ ideas to biopsy or maybe not

 $00:09:32.149 \longrightarrow 00:09:33.618$ as good ideas to biopsy for.

NOTE Confidence: 0.85854478944444

 $00:09:33.620 \longrightarrow 00:09:35.748$ And I put green arrows next to the

NOTE Confidence: 0.85854478944444

 $00:09:35.748 \rightarrow 00:09:37.569$ scenarios where we're more likely to

NOTE Confidence: 0.85854478944444

 $00:09:37.569 \rightarrow 00:09:39.417$ make the diagnosis of myocarditis and

NOTE Confidence: 0.85854478944444

 $00:09:39.479 \dashrightarrow 00:09:41.396$ the ones at the top and the ones here

NOTE Confidence: 0.85854478944444

 $00{:}09{:}41.396 \dashrightarrow 00{:}09{:}44.370$ as well are new onset heart failure.

NOTE Confidence: 0.85854478944444

 $00:09:44.370 \longrightarrow 00:09:46.326$ Of either less than two weeks

NOTE Confidence: 0.85854478944444

 $00:09:46.326 \longrightarrow 00:09:48.422$ duration or two weeks to three

NOTE Confidence: 0.85854478944444

 $00{:}09{:}48{.}422 \dashrightarrow 00{:}09{:}50{.}242$ months duration can be associated

NOTE Confidence: 0.85854478944444

 $00:09:50.242 \longrightarrow 00:09:52.359$ with a dilated left ventricle,

NOTE Confidence: 0.85854478944444

 $00:09:52.360 \rightarrow 00:09:54.560$ new ventricular arrhythmias and then

NOTE Confidence: 0.85854478944444

 $00:09:54.560 \dashrightarrow 00:09:57.372$ here it's basically the same duration

NOTE Confidence: 0.85854478944444

 $00:09:57.372 \rightarrow 00:09:59.536$ with some other symptomatology.

NOTE Confidence: 0.85854478944444

 $00{:}09{:}59{.}540 \dashrightarrow 00{:}10{:}02{.}500$ So those scenarios are good times to look

NOTE Confidence: 0.85854478944444

 $00{:}10{:}02{.}500$ --> $00{:}10{:}05{.}385$ for myocarditis, new onset myocarditis.

00:10:05.385 --> 00:10:07.530 In a patient.

NOTE Confidence: 0.85854478944444

00:10:07.530 --> 00:10:11.224 No evidence was listed as AB or C&
amp; A is

NOTE Confidence: 0.85854478944444

 $00:10:11.224 \rightarrow 00:10:13.846$ like your best evidence like randomized

NOTE Confidence: 0.85854478944444

 $00:10:13.846 \rightarrow 00:10:16.729$ control trials with placebos and all that.

NOTE Confidence: 0.85854478944444

 $00:10:16.730 \longrightarrow 00:10:18.410$ There aren't any or at least

NOTE Confidence: 0.85854478944444

 $00:10:18.410 \longrightarrow 00:10:19.879$ there weren't any of 2007.

NOTE Confidence: 0.85854478944444

 $00{:}10{:}19{.}879 \dashrightarrow 00{:}10{:}21{.}973$ So then B was other trials

NOTE Confidence: 0.85854478944444

 $00{:}10{:}21{.}973 \dashrightarrow 00{:}10{:}24{.}690$ and C was experts best guess.

NOTE Confidence: 0.85854478944444

 $00:10:24.690 \rightarrow 00:10:26.910$ And so you can see that even then

NOTE Confidence: 0.85854478944444

 $00{:}10{:}26{.}910 \dashrightarrow 00{:}10{:}29{.}430$ there was a lot of experts best

NOTE Confidence: 0.85854478944444

 $00{:}10{:}29{.}430 \dashrightarrow 00{:}10{:}32{.}460$ guess as to when we're good good

NOTE Confidence: 0.85854478944444

 $00:10:32.460 \longrightarrow 00:10:34.240$ times to perform biopsies.

NOTE Confidence: 0.85854478944444

 $00:10:34.240 \longrightarrow 00:10:36.196$ Another approach that people have is

NOTE Confidence: 0.85854478944444

00:10:36.196 --> 00:10:38.878 to do this by imaging cardiac MRI.

NOTE Confidence: 0.85854478944444

00:10:38.880 --> 00:10:40.777 And so they went to Lake Louise,

 $00:10:40.780 \longrightarrow 00:10:43.228$ which is a beautiful place up in Canada

NOTE Confidence: 0.85854478944444

 $00:10:43.228 \rightarrow 00:10:46.017$ and came up with the Lake Louise criteria.

NOTE Confidence: 0.85854478944444

 $00:10:46.020 \rightarrow 00:10:47.000$ A few years later,

NOTE Confidence: 0.85854478944444

00:10:47.000 - 00:10:48.225 needing an excuse to probably

NOTE Confidence: 0.85854478944444

00:10:48.225 --> 00:10:49.338 go back to the lake,

NOTE Confidence: 0.85854478944444

 $00{:}10{:}49{.}340 \dashrightarrow 00{:}10{:}51{.}830$ they came back with revised Lake

NOTE Confidence: 0.85854478944444

 $00:10:51.830 \rightarrow 00:10:53.966$ Louise criteria which were improved

NOTE Confidence: 0.85854478944444

 $00:10:53.966 \rightarrow 00:10:56.372$ over the original criteria and these

NOTE Confidence: 0.85854478944444

 $00:10:56.372 \rightarrow 00:10:59.340$ used T1 and T2 imaging of the heart.

NOTE Confidence: 0.85854478944444

 $00:10:59.340 \rightarrow 00:11:02.130$ So on the left we see a T1 weighted

NOTE Confidence: 0.85854478944444

 $00{:}11{:}02{.}130 \dashrightarrow 00{:}11{:}04{.}590$ inversion recovery with Lake gadolinium.

NOTE Confidence: 0.85854478944444

 $00{:}11{:}04{.}590 \dashrightarrow 00{:}11{:}06{.}350$ Enhancement and the orthogonal short

NOTE Confidence: 0.85854478944444

 $00{:}11{:}06{.}350 \dashrightarrow 00{:}11{:}08{.}717$ axis view and what they're seeing I

NOTE Confidence: 0.85854478944444

 $00:11:08.717 \longrightarrow 00:11:10.909$ believe is this pattern here in the wall

NOTE Confidence: 0.7930303446666667

 $00:11:10.965 \rightarrow 00:11:13.114$ here this is T2 mapping which highlights

NOTE Confidence: 0.7930303446666667

 $00{:}11{:}13{.}114 \dashrightarrow 00{:}11{:}15{.}452$ fluid and it's showing mid wall edema.

00:11:15.452 --> 00:11:17.990 So in this black circle you see

NOTE Confidence: 0.7930303446666667

00:11:17.990 --> 00:11:20.066 a little extra fluid that little

NOTE Confidence: 0.7930303446666667

 $00:11:20.066 \longrightarrow 00:11:22.378$ pale area and in that same area

NOTE Confidence: 0.7930303446666667

00:11:22.378 --> 00:11:24.690 again on T1 weighted inversion

NOTE Confidence: 0.7930303446666667

 $00{:}11{:}24.690 \dashrightarrow 00{:}11{:}26.970$ recovery Lake gadolinium enhancement

NOTE Confidence: 0.7930303446666667

 $00:11:26.970 \longrightarrow 00:11:29.838$ shows that same area of edema.

NOTE Confidence: 0.7930303446666667

 $00:11:29.840 \rightarrow 00:11:33.640$ So putting these features together a good.

NOTE Confidence: 0.793030344666667

00:11:33.640 --> 00:11:34.880 I'll just.

NOTE Confidence: 0.888436602941176

 $00{:}12{:}04{.}460 \dashrightarrow 00{:}12{:}06{.}842$ Sometimes I feel that these criteria

NOTE Confidence: 0.888436602941176

 $00:12:06.842 \rightarrow 00:12:09.104$ get used in scenarios where they

NOTE Confidence: 0.888436602941176

 $00:12:09.104 \longrightarrow 00:12:11.724$ may not be as useful a well known.

NOTE Confidence: 0.888436602941176

 $00{:}12{:}11.724 \dashrightarrow 00{:}12{:}13.196$ Scenario where this occurred

NOTE Confidence: 0.888436602941176

 $00:12:13.196 \rightarrow 00:12:15.559$ was in the setting of COVID,

NOTE Confidence: 0.888436602941176

 $00{:}12{:}15{.}560 \dashrightarrow 00{:}12{:}17{.}456$ and so a very influential paper

NOTE Confidence: 0.888436602941176

 $00:12:17.456 \rightarrow 00:12:19.798$ came out in the summer of 2020,

 $00:12:19.800 \longrightarrow 00:12:21.522$ just a few months after COVID

NOTE Confidence: 0.888436602941176

 $00{:}12{:}21{.}522 \dashrightarrow 00{:}12{:}23{.}080$ really became a big thing.

NOTE Confidence: 0.888436602941176

00:12:23.080 --> 00:12:24.720 This came out of Germany,

NOTE Confidence: 0.888436602941176

00:12:24.720 --> 00:12:26.768 and it was a study of 100 patients

NOTE Confidence: 0.888436602941176

 $00:12:26.768 \rightarrow 00:12:29.120$ who had just recovered from COVID-19.

NOTE Confidence: 0.888436602941176

00:12:29.120 --> 00:12:31.660 Cardiac MRI revealed that 78%

NOTE Confidence: 0.888436602941176

00:12:31.660 - 00:12:33.640 of them had cardiac involvement,

NOTE Confidence: 0.888436602941176

 $00{:}12{:}33.640 \dashrightarrow 00{:}12{:}36.388$ and cardiac MRI suggested that 60%

NOTE Confidence: 0.888436602941176

 $00:12:36.388 \rightarrow 00:12:39.140$ had ongoing myocardial inflammation.

NOTE Confidence: 0.888436602941176

 $00:12:39.140 \longrightarrow 00:12:42.255$ So 60% of people who had COVID,

NOTE Confidence: 0.888436602941176

 $00{:}12{:}42.260 \dashrightarrow 00{:}12{:}45.926$ they claim now. Had. No.

NOTE Confidence: 0.888436602941176

 $00:12:45.926 \longrightarrow 00:12:49.740$ Per diem. I to a lot of us,

NOTE Confidence: 0.888436602941176

00:12:49.740 --> 00:12:51.636 I remember calling my cardiology colleagues,

NOTE Confidence: 0.888436602941176

00:12:51.640 --> 00:12:53.530 I said, are you seeing 6 of 10 patients

NOTE Confidence: 0.888436602941176

00:12:53.530 --> 00:12:55.208 who had COVID having myocarditis?

NOTE Confidence: 0.888436602941176

 $00:12:55.210 \rightarrow 00:12:56.380$ And they said, no, we're not,

- NOTE Confidence: 0.888436602941176
- $00:12:56.380 \longrightarrow 00:12:58.240$ we're not seeing this at all.
- NOTE Confidence: 0.888436602941176
- 00:12:58.240 --> 00:13:00.158 I, I and others became very upset.
- NOTE Confidence: 0.888436602941176
- $00{:}13{:}00{.}160 \dashrightarrow 00{:}13{:}01{.}700$ I reached out to circulation and said
- NOTE Confidence: 0.888436602941176
- $00:13:01.700 \rightarrow 00:13:03.677$ we got to write something about this.
- NOTE Confidence: 0.888436602941176
- 00:13:03.680 --> 00:13:05.556 And I got a note back saying,
- NOTE Confidence: 0.888436602941176
- 00:13:05.560 --> 00:13:06.740 yeah, you can write something,
- NOTE Confidence: 0.888436602941176
- $00:13:06.740 \longrightarrow 00:13:08.658$ but you can't do a hit piece
- NOTE Confidence: 0.888436602941176
- $00:13:08.658 \longrightarrow 00:13:10.380$ or takedown of that article.
- NOTE Confidence: 0.888436602941176
- 00:13:10.380 --> 00:13:12.388 So we, we kind of talked around it,
- NOTE Confidence: 0.888436602941176
- $00:13:12.390 \longrightarrow 00:13:14.340$ but other people went after
- NOTE Confidence: 0.888436602941176
- $00:13:14.340 \longrightarrow 00:13:15.120$ this specifically.
- NOTE Confidence: 0.888436602941176
- $00:13:15.120 \longrightarrow 00:13:16.638$ And one of the problems was
- NOTE Confidence: 0.888436602941176
- $00:13:16.638 \longrightarrow 00:13:17.920$ when this paper came out.
- NOTE Confidence: 0.888436602941176
- 00:13:17.920 --> 00:13:19.620 In the middle of 2020,
- NOTE Confidence: 0.888436602941176
- $00{:}13{:}19{.}620 \dashrightarrow 00{:}13{:}21{.}268$ we didn't have a lot of data to
- NOTE Confidence: 0.888436602941176

 $00:13:21.268 \longrightarrow 00:13:22.668$ prove that they weren't right,

NOTE Confidence: 0.888436602941176

00:13:22.670 --> 00:13:24.350 and again, it just seemed,

NOTE Confidence: 0.888436602941176

00:13:24.350 --> 00:13:27.848 anecdotally, really excessive.

NOTE Confidence: 0.888436602941176

00:13:27.850 --> 00:13:29.938 So I was able to work with Rick

NOTE Confidence: 0.888436602941176

 $00{:}13{:}29{.}938 \dashrightarrow 00{:}13{:}31{.}944$ Vanderheide who was at LSU at the time

NOTE Confidence: 0.888436602941176

 $00:13:31.944 \rightarrow 00:13:34.067$ and we collected all of the autopsy data.

NOTE Confidence: 0.888436602941176

 $00:13:34.070 \longrightarrow 00:13:36.440$ We could get all the autopsy

NOTE Confidence: 0.888436602941176

 $00:13:36.440 \rightarrow 00:13:38.709$ series that were coming out with

NOTE Confidence: 0.888436602941176

 $00{:}13{:}38{.}710 \dashrightarrow 00{:}13{:}40{.}714$ 102030 cases from around the world

NOTE Confidence: 0.888436602941176

 $00:13:40.714 \rightarrow 00:13:42.552$ and say what's the incidence

NOTE Confidence: 0.888436602941176

 $00{:}13{:}42.552 \dashrightarrow 00{:}13{:}44.707$ of myocarditis and these cases.

NOTE Confidence: 0.888436602941176

 $00{:}13{:}44.710 \dashrightarrow 00{:}13{:}46.310$ So these are people who died of COVID,

NOTE Confidence: 0.888436602941176

 $00:13:46.310 \rightarrow 00:13:47.741$ so severe COVID,

NOTE Confidence: 0.888436602941176

00:13:47.741 - 00:13:50.603 how much myocarditis are we seeing?

NOTE Confidence: 0.888436602941176

 $00{:}13{:}50{.}610 \dashrightarrow 00{:}13{:}52{.}930$ And the answer was that we felt the

NOTE Confidence: 0.888436602941176

 $00:13:52.930 \rightarrow 00:13:54.936$ true prevalence of myocarditis based on

 $00:13:54.936 \rightarrow 00:13:56.982$ these autopsy series was much lower,

NOTE Confidence: 0.888436602941176

 $00:13:56.990 \longrightarrow 00:13:57.700$ probably less.

NOTE Confidence: 0.888436602941176

00:13:57.700 --> 00:13:58.410 And 2%,

NOTE Confidence: 0.888436602941176

 $00{:}13{:}58{.}410 \dashrightarrow 00{:}14{:}00{.}944$ which seems to be more reasonable relative

NOTE Confidence: 0.888436602941176

 $00{:}14{:}00{.}944 \dashrightarrow 00{:}14{:}03{.}592$ to data that has come since that time.

NOTE Confidence: 0.888436602941176

 $00:14:03.600 \rightarrow 00:14:05.049$ Now we noticed a couple other things

NOTE Confidence: 0.888436602941176

 $00:14:05.049 \rightarrow 00:14:06.520$ when we were doing this project.

NOTE Confidence: 0.888436602941176

 $00:14:06.520 \rightarrow 00:14:08.774$ One is that people were using those

NOTE Confidence: 0.888436602941176

 $00{:}14{:}08{.}774 \dashrightarrow 00{:}14{:}10{.}900$ Dallas criteria that I mentioned before,

NOTE Confidence: 0.888436602941176

 $00:14:10.900 \rightarrow 00:14:13.130$ something we use for endomyocardial

NOTE Confidence: 0.888436602941176

 $00{:}14{:}13.130 \dashrightarrow 00{:}14{:}16.586$ biopsy to make the diagnosis on X or

NOTE Confidence: 0.888436602941176

 $00:14:16.586 \rightarrow 00:14:18.500$ deceased people's hearts, autopsy hearts.

NOTE Confidence: 0.888436602941176

 $00{:}14{:}18{.}500 \dashrightarrow 00{:}14{:}20{.}780$ And it's not designed for that.

NOTE Confidence: 0.888436602941176

 $00{:}14{:}20.780 \dashrightarrow 00{:}14{:}22.680$ It's designed specifically for biopsy.

NOTE Confidence: 0.888436602941176

 $00{:}14{:}22.680 \dashrightarrow 00{:}14{:}24.872$ So that was in appropriate.

- $00:14:24.872 \rightarrow 00:14:25.420$ Secondly,
- NOTE Confidence: 0.888436602941176
- $00{:}14{:}25{.}420 \dashrightarrow 00{:}14{:}26{.}480$ in a lot of series,
- NOTE Confidence: 0.888436602941176
- $00:14:26.480 \rightarrow 00:14:29.978$ people were suggesting they had seen.
- NOTE Confidence: 0.888436602941176
- $00:14:29.980 \rightarrow 00:14:32.176$ Myocarditis and showed a picture of
- NOTE Confidence: 0.888436602941176
- $00{:}14{:}32{.}176 \dashrightarrow 00{:}14{:}34{.}460$ what they described as myocarditis.
- NOTE Confidence: 0.888436602941176
- $00:14:34.460 \longrightarrow 00:14:35.832$ But you look at that picture and
- NOTE Confidence: 0.888436602941176
- $00:14:35.832 \rightarrow 00:14:36.982$ say that's really not myocarditis
- NOTE Confidence: 0.888436602941176
- $00{:}14{:}36{.}982 \dashrightarrow 00{:}14{:}37{.}759$ and there's some,
- NOTE Confidence: 0.888436602941176
- $00:14:37.760 \rightarrow 00:14:39.816$ maybe a few more immune cells than expected,
- NOTE Confidence: 0.888436602941176
- $00:14:39.820 \longrightarrow 00:14:41.836$ but we're not seeing the right
- NOTE Confidence: 0.888436602941176
- $00:14:41.836 \longrightarrow 00:14:42.844$ features for myocarditis.
- NOTE Confidence: 0.888436602941176
- $00{:}14{:}42.850 \dashrightarrow 00{:}14{:}44.460$ And if you're showing me a picture,
- NOTE Confidence: 0.888436602941176
- $00:14:44.460 \rightarrow 00:14:46.371$ I would think you'd be taking the
- NOTE Confidence: 0.888436602941176
- $00:14:46.371 \longrightarrow 00:14:48.270$ most obvious part of the myocarditis.
- NOTE Confidence: 0.888436602941176
- $00{:}14{:}48{.}270 \dashrightarrow 00{:}14{:}49{.}936$ So it LED us to believe that
- NOTE Confidence: 0.888436602941176
- $00:14:49.936 \longrightarrow 00:14:51.240$ even in this scenario,

- NOTE Confidence: 0.888436602941176
- $00:14:51.240 \rightarrow 00:14:52.580$ some people were misusing
- NOTE Confidence: 0.888436602941176
- $00{:}14{:}52{.}580 \dashrightarrow 00{:}14{:}54{.}590$ the tools that we have to
- NOTE Confidence: 0.8880300666666667
- $00{:}14{:}54{.}662 \dashrightarrow 00{:}14{:}56{.}897$ make the diagnosis of myocarditis.
- NOTE Confidence: 0.8880300666666667
- $00:14:56.900 \longrightarrow 00:15:00.250$ So that is a challenge.
- NOTE Confidence: 0.8880300666666667
- $00:15:00.250 \longrightarrow 00:15:02.254$ Some people have to make the
- NOTE Confidence: 0.8880300666666667
- 00:15:02.254 --> 00:15:03.590 diagnosis of myocarditis purely
- NOTE Confidence: 0.8880300666666667
- $00:15:03.647 \longrightarrow 00:15:05.147$ based on clinical features.
- NOTE Confidence: 0.8880300666666667
- 00:15:05.150 --> 00:15:07.250 No access to cardiac MRI,
- NOTE Confidence: 0.8880300666666667
- $00{:}15{:}07{.}250 \dashrightarrow 00{:}15{:}10{.}370$ no access to endomy ocardial biopsy.
- NOTE Confidence: 0.8880300666666667
- $00{:}15{:}10.370 \dashrightarrow 00{:}15{:}11.690$ And these features include chest
- NOTE Confidence: 0.8880300666666667
- 00:15:11.690 --> 00:15:13.430 pain like I talked about earlier,
- NOTE Confidence: 0.8880300666666667
- 00:15:13.430 --> 00:15:16.550 St segment elevation on an EKG,
- NOTE Confidence: 0.8880300666666667
- $00:15:16.550 \longrightarrow 00:15:18.182$ elevations of erythrocyte
- NOTE Confidence: 0.8880300666666667
- 00:15:18.182 --> 00:15:20.358 sedimentation rate or CRP,
- NOTE Confidence: 0.8880300666666667
- 00:15:20.360 --> 00:15:22.832 high sensitivity troponin or
- NOTE Confidence: 0.8880300666666667

 $00{:}15{:}22.832 \dashrightarrow 00{:}15{:}26.540$ elevated CKMB NT Pro BNP elevations

NOTE Confidence: 0.8880300666666667

 $00:15:26.641 \longrightarrow 00:15:29.248$ and cardiac autoantibodies.

NOTE Confidence: 0.8880300666666667

00:15:29.250 --> 00:15:29.784 However,

NOTE Confidence: 0.8880300666666667

 $00:15:29.784 \rightarrow 00:15:32.988$ all of these are nonspecific findings.

NOTE Confidence: 0.8880300666666667

 $00{:}15{:}32{.}990 \dashrightarrow 00{:}15{:}35{.}915$ So you can see all of these in other

NOTE Confidence: 0.8880300666666667

 $00{:}15{:}35{.}915 \dashrightarrow 00{:}15{:}37{.}390$ cardiovascular related diseases.

NOTE Confidence: 0.8880300666666667

 $00:15:37.390 \longrightarrow 00:15:39.460$ Chest pain you obviously can

NOTE Confidence: 0.8880300666666667

 $00:15:39.460 \longrightarrow 00:15:41.116$ see a myocardial infarction.

NOTE Confidence: 0.8880300666666667

 $00{:}15{:}41{.}120 \dashrightarrow 00{:}15{:}43{.}100$ Have that in a ortic dissection.

NOTE Confidence: 0.8880300666666667

00:15:43.100 --> 00:15:44.220 People even complain of

NOTE Confidence: 0.8880300666666667

 $00:15:44.220 \rightarrow 00:15:45.620$ chest pain who have GERD,

NOTE Confidence: 0.8880300666666667

 $00:15:45.620 \longrightarrow 00:15:47.840$ so not the most specific thing.

NOTE Confidence: 0.8880300666666667

 $00{:}15{:}47.840 \dashrightarrow 00{:}15{:}50.206$ And all the other features can be

NOTE Confidence: 0.8880300666666667

 $00:15:50.206 \rightarrow 00:15:52.429$ seen in other either myocardial

NOTE Confidence: 0.8880300666666667

 $00:15:52.429 \rightarrow 00:15:54.685$ infarctions or heart failure.

NOTE Confidence: 0.8880300666666667

 $00:15:54.690 \longrightarrow 00:15:56.650$ So we all got excited last year

- NOTE Confidence: 0.8880300666666667
- 00:15:56.650 --> 00:15:58.645 when a paper came out describing
- NOTE Confidence: 0.8880300666666667
- $00{:}15{:}58.645 \dashrightarrow 00{:}16{:}00.823$ a new blood based biomarker which
- NOTE Confidence: 0.8880300666666667
- $00{:}16{:}00{.}823 \dashrightarrow 00{:}16{:}03{.}816$ was initially called HSA Mirror
- NOTE Confidence: 0.8880300666666667
- $00{:}16{:}03.816 \dashrightarrow 00{:}16{:}05.870$ chromosome 896 and I want to
- NOTE Confidence: 0.8880300666666667
- $00:16:05.870 \rightarrow 00:16:07.490$ spend a moment talking about this.
- NOTE Confidence: 0.8880300666666667
- $00{:}16{:}07{.}490 \dashrightarrow 00{:}16{:}09{.}682$ So this came out in the New England
- NOTE Confidence: 0.8880300666666667
- 00:16:09.682 --> 00:16:12.890 Journal of Medicine in May of 2021.
- NOTE Confidence: 0.8880300666666667
- $00{:}16{:}12.890 \dashrightarrow 00{:}16{:}13.259$ And it was.
- NOTE Confidence: 0.764091064166667
- $00{:}16{:}16{.}250 \dashrightarrow 00{:}16{:}18{.}260$ Called the novel circulating micro RNA
- NOTE Confidence: 0.764091064166667
- $00:16:18.260 \rightarrow 00:16:20.689$ for the detection of acute myocarditis.
- NOTE Confidence: 0.764091064166667
- $00:16:20.690 \longrightarrow 00:16:21.698$ Within just a couple of days
- NOTE Confidence: 0.764091064166667
- $00:16:21.698 \longrightarrow 00:16:22.550$ of this paper coming out,
- NOTE Confidence: 0.764091064166667
- $00{:}16{:}22.550 \dashrightarrow 00{:}16{:}23.760$ I've gotten multiple emails from
- NOTE Confidence: 0.764091064166667
- $00{:}16{:}23.760 \dashrightarrow 00{:}16{:}25.250$ colleagues from all over the place.
- NOTE Confidence: 0.764091064166667
- 00:16:25.250 --> 00:16:27.105 Hey, Mark, have you seen this paper?
- NOTE Confidence: 0.764091064166667

 $00:16:27.110 \longrightarrow 00:16:28.629$ And the reason they asked is because,

NOTE Confidence: 0.764091064166667

00:16:28.630 --> 00:16:30.034 well, I'm a cardiova
scular $\,$

NOTE Confidence: 0.764091064166667

00:16:30.034 --> 00:16:32.075 pathologist and I do micro RNA's.

NOTE Confidence: 0.764091064166667

 $00:16:32.075 \rightarrow 00:16:34.070$ And so that's clearly in my wheelhouse

NOTE Confidence: 0.764091064166667

 $00:16:34.070 \longrightarrow 00:16:36.248$ of things that I would be interested in.

NOTE Confidence: 0.764091064166667

00:16:36.250 --> 00:16:37.438 And I was like, yeah, thank you.

NOTE Confidence: 0.764091064166667

 $00:16:37.438 \rightarrow 00:16:40.570$ I did see it and I'm reading it right now.

NOTE Confidence: 0.764091064166667

 $00{:}16{:}40{.}570 \dashrightarrow 00{:}16{:}42{.}874$ And So what they did was they started

NOTE Confidence: 0.764091064166667

 $00{:}16{:}42.874 \dashrightarrow 00{:}16{:}44.925$ with a mouse and it's known that

NOTE Confidence: 0.764091064166667

00:16:44.925 --> 00:16:47.583 TH 17 cells and a type of immune

NOTE Confidence: 0.764091064166667

 $00{:}16{:}47{.}583 \dashrightarrow 00{:}16{:}49{.}548$ cell is increased in myocarditis.

NOTE Confidence: 0.764091064166667

 $00{:}16{:}49{.}550 \dashrightarrow 00{:}16{:}52{.}784$ And they found a micro RNA called

NOTE Confidence: 0.764091064166667

 $00:16:52.784 \longrightarrow 00:16:55.865$ mere 721 and micronas are just

NOTE Confidence: 0.764091064166667

 $00{:}16{:}55{.}865 \dashrightarrow 00{:}16{:}58{.}988$ numbered short RNA's 21 bases or so.

NOTE Confidence: 0.764091064166667

 $00{:}16{:}58{.}990 \dashrightarrow 00{:}17{:}00{.}446$ And I could go into much more detail,

NOTE Confidence: 0.764091064166667

 $00:17:00.450 \longrightarrow 00:17:02.130$ but I'll try and keep it simple.

 $00:17:02.130 \longrightarrow 00:17:04.874$ They found that this mere 721 in

NOTE Confidence: 0.764091064166667

 $00{:}17{:}04.874 \dashrightarrow 00{:}17{:}07.346$ mice was elevated in myocarditis as

NOTE Confidence: 0.764091064166667

 $00{:}17{:}07{.}346 \dashrightarrow 00{:}17{:}10.679$ seen here and it was not elevated

NOTE Confidence: 0.764091064166667

 $00:17:10.679 \longrightarrow 00:17:12.134$ in mycardial infarctions.

NOTE Confidence: 0.764091064166667

 $00:17:12.140 \longrightarrow 00:17:13.236$ That was pretty exciting.

NOTE Confidence: 0.764091064166667

 $00{:}17{:}13.236 \dashrightarrow 00{:}17{:}14.455$ They then said, well,

NOTE Confidence: 0.764091064166667

 $00:17:14.455 \rightarrow 00:17:17.615$ what's the human correlate of that micro RNA?

NOTE Confidence: 0.764091064166667

 $00:17:17.620 \longrightarrow 00:17:19.318$ And they found a sequence on

NOTE Confidence: 0.764091064166667

 $00{:}17{:}19{.}318 \dashrightarrow 00{:}17{:}21{.}219$ chromosome 8 which they felt matched.

NOTE Confidence: 0.764091064166667

 $00{:}17{:}21{.}220 \dashrightarrow 00{:}17{:}24{.}208$ And then they showed across multiple

NOTE Confidence: 0.764091064166667

 $00{:}17{:}24.208 \dashrightarrow 00{:}17{:}27.784$ other cohorts that this micro RNA in

NOTE Confidence: 0.764091064166667

 $00{:}17{:}27.784 \dashrightarrow 00{:}17{:}30.274$ humans was elevated in myocarditis.

NOTE Confidence: 0.764091064166667

 $00{:}17{:}30{.}280 \dashrightarrow 00{:}17{:}33{.}104$ You can see that even normals had some

NOTE Confidence: 0.764091064166667

 $00:17:33.104 \rightarrow 00:17:35.656$ expression of this mere chromosome 896,

NOTE Confidence: 0.764091064166667

 $00:17:35.656 \rightarrow 00:17:38.568$ but again, it was elevated in myocarditis.

 $00:17:38.570 \longrightarrow 00:17:40.360$ So this paper came out.

NOTE Confidence: 0.764091064166667

00:17:40.360 --> 00:17:41.820 I think I got excited.

NOTE Confidence: 0.764091064166667

 $00{:}17{:}41.820 \dashrightarrow 00{:}17{:}42.771$ I had already.

NOTE Confidence: 0.764091064166667

 $00:17:42.771 \longrightarrow 00:17:44.673$ Published a paper saying use of

NOTE Confidence: 0.764091064166667

00:17:44.673 --> 00:17:46.136 micrornas as cardiovascular biomarkers

NOTE Confidence: 0.764091064166667

 $00{:}17{:}46.136 \dashrightarrow 00{:}17{:}48.670$ and we specifically said this is an

NOTE Confidence: 0.764091064166667

 $00:17:48.733 \rightarrow 00:17:50.910$ area where they might be useful where

NOTE Confidence: 0.764091064166667

 $00:17:50.910 \rightarrow 00:17:52.705$ some other places they wouldn't be.

NOTE Confidence: 0.764091064166667

00:17:52.705 --> 00:17:54.700 And at the time I was studying

NOTE Confidence: 0.764091064166667

00:17:54.766 --> 00:17:56.668 micro RNA expression in the lab,

NOTE Confidence: 0.764091064166667

 $00{:}17{:}56.670 \dashrightarrow 00{:}17{:}59.538$ we had huge datasets of cellular

NOTE Confidence: 0.764091064166667

 $00{:}17{:}59{.}538 \dashrightarrow 00{:}18{:}01{.}450$ microrna expression from sequencing.

NOTE Confidence: 0.764091064166667

 $00{:}18{:}01{.}450 \dashrightarrow 00{:}18{:}04{.}483$ And I reached out to my postdoc a room

NOTE Confidence: 0.764091064166667

00:18:04.483 --> 00:18:06.946 and I said Arun, let's find this sequence,

NOTE Confidence: 0.764091064166667

 $00:18:06.946 \rightarrow 00:18:08.566$ let's see where it's expressed.

NOTE Confidence: 0.764091064166667

00:18:08.570 --> 00:18:10.826 Just TH 17 cells or is it found

- NOTE Confidence: 0.764091064166667
- $00:18:10.826 \rightarrow 00:18:12.668$ in other cells like let's?
- NOTE Confidence: 0.764091064166667
- $00:18:12.670 \longrightarrow 00:18:13.492$ Let's solve this.
- NOTE Confidence: 0.764091064166667
- $00:18:13.492 \rightarrow 00:18:15.136$ So I sent them scurrying away.
- NOTE Confidence: 0.764091064166667
- 00:18:15.140 --> 00:18:16.736 He comes back a little later
- NOTE Confidence: 0.764091064166667
- $00:18:16.736 \longrightarrow 00:18:18.150$ that day and says Mark.
- NOTE Confidence: 0.764091064166667
- 00:18:18.150 --> 00:18:19.074 I don't see it.
- NOTE Confidence: 0.764091064166667
- 00:18:19.074 --> 00:18:21.250 I can't find it in any of our data.
- NOTE Confidence: 0.764091064166667
- 00:18:21.250 --> 00:18:23.636 I said whoa, whoa, whoa, this is weird.
- NOTE Confidence: 0.764091064166667
- $00{:}18{:}23.636 \dashrightarrow 00{:}18{:}25.710$ Let me go look further at this paper.
- NOTE Confidence: 0.764091064166667
- $00:18:25.710 \longrightarrow 00:18:28.368$ So it turned out there's some
- NOTE Confidence: 0.764091064166667
- 00:18:28.368 --> 00:18:30.730 real problems with this paper,
- NOTE Confidence: 0.764091064166667
- $00:18:30.730 \longrightarrow 00:18:32.638$ which essentially is that
- NOTE Confidence: 0.764091064166667
- 00:18:32.638 --> 00:18:34.546 this sequence doesn't exist.
- NOTE Confidence: 0.764091064166667
- $00{:}18{:}34{.}550 \dashrightarrow 00{:}18{:}36{.}290$ There was no micro RNA.
- NOTE Confidence: 0.764091064166667
- $00:18:36.290 \rightarrow 00:18:39.890$ There's no HSA chromosome 896.
- NOTE Confidence: 0.764091064166667

00:18:39.890 --> 00:18:41.750 A couple things to point out

NOTE Confidence: 0.764091064166667

 $00:18:41.750 \longrightarrow 00:18:42.990$ here on the left.

NOTE Confidence: 0.764091064166667

 $00:18:42.990 \longrightarrow 00:18:45.768$ This is a normal micro RNA

NOTE Confidence: 0.764091064166667

 $00:18:45.768 \longrightarrow 00:18:48.190$ structure that you see this.

NOTE Confidence: 0.764091064166667

00:18:48.190 --> 00:18:49.828 It has a hairpin loop of

NOTE Confidence: 0.764091064166667

 $00:18:49.828 \longrightarrow 00:18:50.647$ roughly this dimension.

NOTE Confidence: 0.764091064166667

 $00:18:50.650 \longrightarrow 00:18:54.048$ This is the classic HSA Mirror 1/26

NOTE Confidence: 0.764091064166667

 $00{:}18{:}54.048 \dashrightarrow 00{:}18{:}57.028$ and abundant well described micro RNA

NOTE Confidence: 0.764091064166667

 $00{:}18{:}57{.}028 \dashrightarrow 00{:}18{:}59{.}220$ which they described in the paper as well.

NOTE Confidence: 0.764091064166667

 $00:18:59.220 \longrightarrow 00:19:03.015$ This is the mouse mirror 721 and this

NOTE Confidence: 0.764091064166667

00:19:03.015 --> 00:19:05.497 is human chromosome chromosome 896,

NOTE Confidence: 0.764091064166667

 $00{:}19{:}05{.}497 \dashrightarrow 00{:}19{:}07{.}519$ which should make a hairpin loop

NOTE Confidence: 0.764091064166667

 $00:19:07.519 \longrightarrow 00:19:09.679$ but has this crazy structure.

NOTE Confidence: 0.764091064166667

 $00:19:09.680 \longrightarrow 00:19:11.521$ So that's not going to be part

NOTE Confidence: 0.764091064166667

00:19:11.521 --> 00:19:12.310 of the micro

NOTE Confidence: 0.893566082666667

 $00:19:12.379 \longrightarrow 00:19:14.219$ RNA machinery to process this.

- NOTE Confidence: 0.893566082666667
- $00:19:14.220 \rightarrow 00:19:16.019$ That was one thing that was weird.
- NOTE Confidence: 0.893566082666667
- $00:19:16.020 \longrightarrow 00:19:19.230$ The second is that mirror.
- NOTE Confidence: 0.893566082666667
- $00{:}19{:}19{.}230 \dashrightarrow 00{:}19{:}21{.}550$ 721 is located in the mouse in the
- NOTE Confidence: 0.893566082666667
- $00:19:21.550 \longrightarrow 00:19:23.688$ locus of a gene called Cux one.
- NOTE Confidence: 0.893566082666667
- $00{:}19{:}23.690 \dashrightarrow 00{:}19{:}25.783$ U sually when a micro RNA is in
- NOTE Confidence: 0.893566082666667
- 00:19:25.783 --> 00:19:28.070 a gene and intragenic region,
- NOTE Confidence: 0.893566082666667
- 00:19:28.070 00:19:30.098 it stays in that same regions,
- NOTE Confidence: 0.893566082666667
- $00:19:30.100 \longrightarrow 00:19:32.938$ particularly over a short time period
- NOTE Confidence: 0.893566082666667
- $00{:}19{:}32{.}938 \dashrightarrow 00{:}19{:}36{.}336$ such as between mice and human and the
- NOTE Confidence: 0.893566082666667
- $00:19:36.336 \longrightarrow 00:19:38.394$ sequence that they identified was on
- NOTE Confidence: 0.893566082666667
- $00:19:38.394 \rightarrow 00:19:40.354$ chromosome 8 and may of corresponded
- NOTE Confidence: 0.893566082666667
- $00{:}19{:}40{.}354 \dashrightarrow 00{:}19{:}42{.}709$ with a long non coding RNA in mice.
- NOTE Confidence: 0.893566082666667
- $00:19:42.710 \longrightarrow 00:19:45.230$ It was definitely found in the
- NOTE Confidence: 0.893566082666667
- $00{:}19{:}45{.}230 \dashrightarrow 00{:}19{:}48{.}039$ area of a long coding RNA.
- NOTE Confidence: 0.893566082666667
- 00:19:48.040 --> 00:19:51.480 Inhuman additionally, and most critically,
- NOTE Confidence: 0.893566082666667

00:19:51.480 --> 00:19:53.223 is a micro RNA has an area

NOTE Confidence: 0.893566082666667

 $00{:}19{:}53{.}223 \dashrightarrow 00{:}19{:}54{.}600$ called a seed sequence,

NOTE Confidence: 0.893566082666667

 $00{:}19{:}54.600 \dashrightarrow 00{:}19{:}57.832$ and this six base or seven base nucleotide

NOTE Confidence: 0.893566082666667

 $00:19:57.832 \rightarrow 00:20:01.117$ sequence at the end is completely invariant.

NOTE Confidence: 0.893566082666667

 $00:20:01.120 \longrightarrow 00:20:03.608$ It's the critical piece for binding of that

NOTE Confidence: 0.893566082666667

00:20:03.608 --> 00:20:06.236 micro RNA to its targets on Messenger RNAs,

NOTE Confidence: 0.893566082666667

 $00:20:06.240 \longrightarrow 00:20:08.683$ and they propose that two of the

NOTE Confidence: 0.893566082666667

 $00:20:08.683 \rightarrow 00:20:10.340$ six nucleotides had changed.

NOTE Confidence: 0.893566082666667

 $00:20:10.340 \longrightarrow 00:20:12.321$ And the analogy that I have for

NOTE Confidence: 0.893566082666667

 $00:20:12.321 \longrightarrow 00:20:13.989$ that is suddenly being able to

NOTE Confidence: 0.893566082666667

 $00:20:13.989 \longrightarrow 00:20:15.760$ use your car key to open your

NOTE Confidence: 0.893566082666667

 $00{:}20{:}15.825 \dashrightarrow 00{:}20{:}17.829$ house through the key rather than.

NOTE Confidence: 0.893566082666667

00:20:17.830 --> 00:20:19.474 Of your house key.

NOTE Confidence: 0.893566082666667

 $00:20:19.474 \rightarrow 00:20:22.407$ It's a massive change in identification and

NOTE Confidence: 0.893566082666667

 $00:20:22.407 \rightarrow 00:20:25.137$ everything would have to move in tandem.

NOTE Confidence: 0.893566082666667

 $00:20:25.140 \longrightarrow 00:20:26.946$ You'd have to switch out all the

- NOTE Confidence: 0.893566082666667
- $00:20:26.946 \longrightarrow 00:20:28.789$ locks in your house at the same
- NOTE Confidence: 0.893566082666667
- 00:20:28.789 --> 00:20:30.301 time to match your car key,
- NOTE Confidence: 0.893566082666667
- $00{:}20{:}30{.}310 \dashrightarrow 00{:}20{:}32{.}230$ and we don't have any evidence of that.
- NOTE Confidence: 0.893566082666667
- $00:20:32.230 \longrightarrow 00:20:34.519$ So there's a lot of concerns in
- NOTE Confidence: 0.893566082666667
- $00:20:34.519 \rightarrow 00:20:36.829$ addition to not finding any reads.
- NOTE Confidence: 0.893566082666667
- $00{:}20{:}36.830 \dashrightarrow 00{:}20{:}38.510$ And when we reached out to a colleague
- NOTE Confidence: 0.893566082666667
- 00:20:38.510 00:20:40.207 who had even more data than we had,
- NOTE Confidence: 0.893566082666667
- $00:20:40.210 \longrightarrow 00:20:43.360$ it wasn't present in 230 billion reads.
- NOTE Confidence: 0.893566082666667
- $00{:}20{:}43.360 \dashrightarrow 00{:}20{:}44.770$ I then additionally I called the
- NOTE Confidence: 0.893566082666667
- 00:20:44.770 --> 00:20:46.120 holistica X Prize on Twitter.
- NOTE Confidence: 0.893566082666667
- 00:20:46.120 --> 00:20:47.488 I said if anyone can find the sequence
- NOTE Confidence: 0.893566082666667
- 00:20:47.488 --> 00:20:49.384 let me know, I'll pay you money.
- NOTE Confidence: 0.893566082666667
- $00{:}20{:}49{.}384 \dashrightarrow 00{:}20{:}52{.}198$ And I had a student from somewhere up
- NOTE Confidence: 0.893566082666667
- $00{:}20{:}52.198 \dashrightarrow 00{:}20{:}55.256$ in this area who found 200 base pair
- NOTE Confidence: 0.893566082666667
- $00{:}20{:}55{.}256 \dashrightarrow 00{:}20{:}57{.}216$ sequence reads and thy roid tissue,
- NOTE Confidence: 0.893566082666667
$00:20:57.220 \rightarrow 00:20:59.266$ again suggesting either this was DNA

NOTE Confidence: 0.893566082666667

00:20:59.266 --> 00:21:01.298 contamination in the RNA sequencing data

NOTE Confidence: 0.893566082666667

00:21:01.298 --> 00:21:03.714 set or it's part of a larger sequence,

NOTE Confidence: 0.893566082666667

 $00:21:03.720 \longrightarrow 00:21:06.060$ but again not a short RNA.

NOTE Confidence: 0.893566082666667

 $00:21:06.060 \longrightarrow 00:21:07.593$ And the reason I'm going on and

NOTE Confidence: 0.893566082666667

 $00:21:07.593 \longrightarrow 00:21:09.422$ on and on about this is because

NOTE Confidence: 0.893566082666667

 $00:21:09.422 \longrightarrow 00:21:10.817$ we put all this together.

NOTE Confidence: 0.893566082666667

 $00:21:10.820 \longrightarrow 00:21:12.040$ We let the Newland Journal

NOTE Confidence: 0.893566082666667

00:21:12.040 --> 00:21:13.260 of Medicine know 8 days.

NOTE Confidence: 0.893566082666667

 $00:21:13.260 \longrightarrow 00:21:15.990$ After the paper came out that they

NOTE Confidence: 0.893566082666667

 $00{:}21{:}15{.}990 \dashrightarrow 00{:}21{:}18{.}119$ were very serious concerns about

NOTE Confidence: 0.893566082666667

00:21:18.119 $\operatorname{-->}$ 00:21:20.771 this thing which was proposed as

NOTE Confidence: 0.893566082666667

00:21:20.771 --> 00:21:23.307 a biomarker and Long story short,

NOTE Confidence: 0.893566082666667

 $00:21:23.310 \longrightarrow 00:21:25.865$ it wasn't put out there to the

NOTE Confidence: 0.893566082666667

 $00:21:25.865 \rightarrow 00:21:27.928$ public until September of this year.

NOTE Confidence: 0.893566082666667

 $00:21:27.930 \longrightarrow 00:21:30.990$ It was of to me embarrassing,

- NOTE Confidence: 0.893566082666667
- $00:21:30.990 \longrightarrow 00:21:33.288$ but they refused to move on.
- NOTE Confidence: 0.893566082666667
- 00:21:33.290 --> 00:21:35.468 This major concern and our major
- NOTE Confidence: 0.893566082666667
- $00:21:35.468 \rightarrow 00:21:37.734$ concern was please don't let anybody
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}37{.}734 \dashrightarrow 00{:}21{:}39{.}609$ study this micro RNA biomarker
- NOTE Confidence: 0.893566082666667
- $00:21:39.609 \rightarrow 00:21:41.568$ because it's not a micro RNA,
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}41{.}570 \dashrightarrow 00{:}21{:}44{.}167$ it's possible and I'm not a purist.
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}44{.}170 \dashrightarrow 00{:}21{:}46{.}648$ That any small RNA sequence that can
- NOTE Confidence: 0.893566082666667
- $00:21:46.648 \rightarrow 00:21:49.670$ serve as a biomarker is a biomarker.
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}49.670 \dashrightarrow 00{:}21{:}52.685$ If we're in green shoes is a good biomarker.
- NOTE Confidence: 0.893566082666667
- $00:21:52.690 \rightarrow 00:21:54.670$ Then let's look at people's shoes.
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}54.670 \dashrightarrow 00{:}21{:}55.686$ I'm fine with that.
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}55{.}686 \dashrightarrow 00{:}21{:}57{.}630$ But there was no connection between the two.
- NOTE Confidence: 0.893566082666667
- $00{:}21{:}57{.}630 \dashrightarrow 00{:}22{:}00{.}158$ So they had about a A1 and 2.5
- NOTE Confidence: 0.893566082666667
- 00:22:00.158 --> 00:22:00.790 billion chance,
- NOTE Confidence: 0.893566082666667
- $00{:}22{:}00{.}790 \dashrightarrow 00{:}22{:}02{.}506$ assuming the number of RNA that
- NOTE Confidence: 0.893566082666667

 $00:22:02.506 \rightarrow 00:22:03.650$ you'd see that they

NOTE Confidence: 0.777480535833333

 $00:22:03.712 \longrightarrow 00:22:06.738$ were right. So a big concern,

NOTE Confidence: 0.777480535833333

 $00{:}22{:}06{.}738 \dashrightarrow 00{:}22{:}09{.}624$ I met with Carlos last night

NOTE Confidence: 0.777480535833333

 $00:22:09.624 \rightarrow 00:22:11.046$ and he also agreed with me.

NOTE Confidence: 0.777480535833333

 $00:22:11.050 \rightarrow 00:22:14.614$ So I felt very vindicated about all of that.

NOTE Confidence: 0.777480535833333

 $00{:}22{:}14.620 \dashrightarrow 00{:}22{:}16.474$ OK. So I want to move on and say

NOTE Confidence: 0.777480535833333

 $00:22:16.474 \longrightarrow 00:22:18.211$ basically that we got excited about a

NOTE Confidence: 0.777480535833333

 $00{:}22{:}18{.}211 \dashrightarrow 00{:}22{:}20{.}078$ biomarker and we don't have a biomarker.

NOTE Confidence: 0.777480535833333

 $00:22:20.080 \longrightarrow 00:22:22.810$ So let's turn our attention

NOTE Confidence: 0.777480535833333

 $00:22:22.810 \longrightarrow 00:22:25.540$ back to the Dallas criteria.

NOTE Confidence: 0.777480535833333

 $00{:}22{:}25{.}540 \dashrightarrow 00{:}22{:}29{.}791$ The Dallas criteria came about circa 1985.

NOTE Confidence: 0.777480535833333

 $00{:}22{:}29{.}791 \dashrightarrow 00{:}22{:}32{.}050$ And the reason for this was at that time

NOTE Confidence: 0.777480535833333

 $00:22:32.104 \rightarrow 00:22:34.127$ they were trying to do clinical trials

NOTE Confidence: 0.777480535833333

 $00:22:34.127 \longrightarrow 00:22:36.214$ of steroids to see if immunosuppression

NOTE Confidence: 0.777480535833333

 $00:22:36.214 \rightarrow 00:22:38.154$ would be useful for myocarditis.

NOTE Confidence: 0.777480535833333

 $00:22:38.160 \longrightarrow 00:22:40.200$ And the problem was that pathologists

 $00{:}22{:}40{.}200 \dashrightarrow 00{:}22{:}42{.}131$ didn't have the same criteria

NOTE Confidence: 0.777480535833333

 $00:22:42.131 \longrightarrow 00:22:43.670$ at different institutions.

NOTE Confidence: 0.777480535833333

 $00{:}22{:}43.670 \dashrightarrow 00{:}22{:}45.506$ People had different things going on,

NOTE Confidence: 0.777480535833333

00:22:45.510 --> 00:22:46.795 and so they brought everybody

NOTE Confidence: 0.777480535833333

 $00:22:46.795 \longrightarrow 00:22:47.566$ together in Dallas.

NOTE Confidence: 0.777480535833333

 $00{:}22{:}47{.}570 \dashrightarrow 00{:}22{:}50{.}090$ They got a bunch of microscopes.

NOTE Confidence: 0.777480535833333

 $00{:}22{:}50.090 \dashrightarrow 00{:}22{:}52.288$ And lots of glass slides of myocarditis

NOTE Confidence: 0.777480535833333

 $00:22:52.288 \rightarrow 00:22:55.133$ and they sat down and hammered out some

NOTE Confidence: 0.777480535833333

00:22:55.133 - > 00:22:57.471 criteria which were published here in 1986.

NOTE Confidence: 0.777480535833333

 $00:22:57.471 \rightarrow 00:22:59.648$ And they basically had these three levels.

NOTE Confidence: 0.777480535833333

 $00:22:59.650 \rightarrow 00:23:02.710$ They had the definition of myocarditis,

NOTE Confidence: 0.777480535833333

 $00{:}23{:}02{.}710 \dashrightarrow 00{:}23{:}04{.}230$ which is myocardial necrosis

NOTE Confidence: 0.777480535833333

 $00{:}23{:}04{.}230 \dashrightarrow 00{:}23{:}06{.}510$ degeneration or both in the absence

NOTE Confidence: 0.777480535833333

 $00{:}23{:}06{.}579 \dashrightarrow 00{:}23{:}08{.}507$ of significant coronary artery

NOTE Confidence: 0.777480535833333

 $00{:}23{:}08{.}507 \dashrightarrow 00{:}23{:}10{.}435$ disease with adjacent inflammatory

 $00:23:10.435 \rightarrow 00:23:12.648$ infiltrate with or without fibrosis,

NOTE Confidence: 0.777480535833333

 $00:23:12.650 \longrightarrow 00:23:13.548$ borderline myocarditis,

NOTE Confidence: 0.777480535833333

 $00{:}23{:}13.548 \dashrightarrow 00{:}23{:}15.793$ which was this intermediate think

NOTE Confidence: 0.777480535833333

00:23:15.793 - 00:23:17.950 of dysplasia as a correlate.

NOTE Confidence: 0.777480535833333

 $00:23:17.950 \longrightarrow 00:23:19.938$ So it's not normal, but it's not.

NOTE Confidence: 0.777480535833333

00:23:19.940 --> 00:23:20.344 Myocarditis,

NOTE Confidence: 0.777480535833333

 $00:23:20.344 \longrightarrow 00:23:22.768$ so we'll just call it borderline

NOTE Confidence: 0.777480535833333

00:23:22.768 --> 00:23:24.810 myocarditis and no myocarditis,

NOTE Confidence: 0.777480535833333

 $00{:}23{:}24.810 \dashrightarrow 00{:}23{:}27.245$ no evidence of inflammation and

NOTE Confidence: 0.777480535833333

 $00{:}23{:}27{.}245 \dashrightarrow 00{:}23{:}29{.}190$ the borderline, somewhat unclear.

NOTE Confidence: 0.777480535833333

 $00{:}23{:}29{.}190 \dashrightarrow 00{:}23{:}31{.}130$ It's inflammatory infiltrate too

NOTE Confidence: 0.777480535833333

 $00:23:31.130 \rightarrow 00:23:33.990$ sparse or mysite damage not apparent.

NOTE Confidence: 0.777480535833333

 $00:23:33.990 \longrightarrow 00:23:35.985$ So we don't know what's too few

NOTE Confidence: 0.777480535833333

 $00:23:35.985 \rightarrow 00:23:37.789$ cells to call it borderline,

NOTE Confidence: 0.777480535833333

 $00:23:37.790 \rightarrow 00:23:40.030$ what's too many cells to call it borderline,

NOTE Confidence: 0.777480535833333

 $00:23:40.030 \longrightarrow 00:23:42.526$ it's just kind of nebulous space.

- NOTE Confidence: 0.777480535833333
- $00:23:42.530 \rightarrow 00:23:44.587$ Again, this is published in 1986.
- NOTE Confidence: 0.777480535833333
- $00:23:44.587 \rightarrow 00:23:46.969$ And if you perform subsequent biopsies,
- NOTE Confidence: 0.777480535833333
- 00:23:46.970 --> 00:23:48.650 which we tend not to do anymore,
- NOTE Confidence: 0.777480535833333
- $00{:}23{:}48.650 \dashrightarrow 00{:}23{:}50.558$ you could diagnose it as ongoing.
- NOTE Confidence: 0.777480535833333
- 00:23:50.560 --> 00:23:52.378 Resolved for resolving,
- NOTE Confidence: 0.777480535833333
- $00:23:52.378 \longrightarrow 00:23:56.620$ so I skipped one in the middle.
- NOTE Confidence: 0.777480535833333
- $00{:}23{:}56{.}620 \dashrightarrow 00{:}24{:}01{.}480$ In 2013, a second set of criteria came about.
- NOTE Confidence: 0.777480535833333
- $00:24:01.480 \longrightarrow 00:24:04.315$ Where the key changes were now to
- NOTE Confidence: 0.777480535833333
- 00:24:04.315 --> 00:24:05.696 introduce immunohistochemistry 1986,
- NOTE Confidence: 0.777480535833333
- $00:24:05.696 \rightarrow 00:24:07.960$ we weren't really doing
- NOTE Confidence: 0.777480535833333
- $00{:}24{:}07{.}960 \dashrightarrow 00{:}24{:}09{.}398$ immunohistochemistry frequently and
- NOTE Confidence: 0.777480535833333
- $00{:}24{:}09{.}398 \dashrightarrow 00{:}24{:}11{.}568$ certainly not on endomy ocardial biopsy.
- NOTE Confidence: 0.777480535833333
- $00{:}24{:}11{.}570 \dashrightarrow 00{:}24{:}13{.}360$ So here a European group,
- NOTE Confidence: 0.777480535833333
- $00{:}24{:}13.360 \dashrightarrow 00{:}24{:}15.250$ the European Society of Cardiology.
- NOTE Confidence: 0.766632917142857
- $00{:}24{:}18{.}280 \dashrightarrow 00{:}24{:}20{.}317$ Made essentially 2 changes to the criteria.
- NOTE Confidence: 0.766632917142857

 $00:24:20.320 \longrightarrow 00:24:22.600$ One was again to implement

NOTE Confidence: 0.766632917142857

00:24:22.600 -> 00:24:23.056 immunohistochemistry,

NOTE Confidence: 0.766632917142857

00:24:23.060 --> 00:24:25.088 looking for CD3 lymphocytes,

NOTE Confidence: 0.766632917142857

 $00{:}24{:}25{.}088 \dashrightarrow 00{:}24{:}28{.}130$ and to define 14 leukocytes per

NOTE Confidence: 0.766632917142857

 $00{:}24{:}28{.}222 \dashrightarrow 00{:}24{:}31{.}026$ millimeter squared as definitive

NOTE Confidence: 0.766632917142857

 $00:24:31.026 \rightarrow 00:24:33.338$ diagnosis of myocarditis. OK.

NOTE Confidence: 0.766632917142857

 $00:24:33.338 \longrightarrow 00:24:35.002$ So that's the setting of what we have.

NOTE Confidence: 0.766632917142857

 $00{:}24{:}35{.}010 \dashrightarrow 00{:}24{:}36{.}898$ We kind of have an old criteria that

NOTE Confidence: 0.766632917142857

00:24:36.898 --> 00:24:38.870 I thought every
body used and a new

NOTE Confidence: 0.766632917142857

 $00{:}24{:}38.870 \dashrightarrow 00{:}24{:}40.570$ criteria that maybe some people use.

NOTE Confidence: 0.766632917142857

 $00{:}24{:}40.570 \dashrightarrow 00{:}24{:}42.646$ Cause I actually wasn't using that.

NOTE Confidence: 0.766632917142857

00:24:42.650 --> 00:24:44.966 And we decided between the Society

NOTE Confidence: 0.766632917142857

00:24:44.966 --> 00:24:46.124 for Cardiovascular Pathology,

NOTE Confidence: 0.766632917142857

 $00{:}24{:}46{.}130 \dashrightarrow 00{:}24{:}48{.}750$ SBP and the European Society,

NOTE Confidence: 0.766632917142857

 $00:24:48.750 \longrightarrow 00:24:50.186$ we should study this.

NOTE Confidence: 0.766632917142857

 $00:24:50.186 \longrightarrow 00:24:51.981$ We should find out what

- NOTE Confidence: 0.766632917142857
- $00{:}24{:}51{.}981 \dashrightarrow 00{:}24{:}53{.}927$ people are using as criteria.
- NOTE Confidence: 0.766632917142857
- $00{:}24{:}53{.}930 \dashrightarrow 00{:}24{:}56{.}522$ So this is now the work of Monica de
- NOTE Confidence: 0.766632917142857
- $00{:}24{:}56{.}522 \dashrightarrow 00{:}24{:}58{.}858$ Gaspari and Chi Lin and I worked with
- NOTE Confidence: 0.766632917142857
- $00:24:58.858 \rightarrow 00:25:01.608$ them where we developed a survey to ask
- NOTE Confidence: 0.766632917142857
- $00:25:01.608 \rightarrow 00:25:03.774$ people about how they diagnose myocarditis.
- NOTE Confidence: 0.766632917142857
- $00{:}25{:}03{.}774 \dashrightarrow 00{:}25{:}05{.}718$ We then sent emails out to
- NOTE Confidence: 0.766632917142857
- $00:25:05.718 \longrightarrow 00:25:07.758$ members of both of our societies.
- NOTE Confidence: 0.766632917142857
- $00{:}25{:}07.760 \dashrightarrow 00{:}25{:}08.928$ We tweeted about it.
- NOTE Confidence: 0.766632917142857
- $00{:}25{:}08{.}928 \dashrightarrow 00{:}25{:}11{.}402$ I sent emails and other people sent directed
- NOTE Confidence: 0.766632917142857
- $00:25:11.402 \longrightarrow 00:25:14.058$ emails to people to ask them to participate.
- NOTE Confidence: 0.766632917142857
- $00:25:14.060 \longrightarrow 00:25:16.046$ And we were thrilled to get
- NOTE Confidence: 0.766632917142857
- $00:25:16.046 \longrightarrow 00:25:17.039$ exactly 100 participants.
- NOTE Confidence: 0.766632917142857
- $00{:}25{:}17.040 \dashrightarrow 00{:}25{:}19.308$ It's so much easier to do math on 100
- NOTE Confidence: 0.766632917142857
- $00{:}25{:}19{.}308 \dashrightarrow 00{:}25{:}22{.}080$ than 101 or 99, and that was great.
- NOTE Confidence: 0.766632917142857
- $00:25:22.080 \dashrightarrow 00:25:24.480$ So we had 100 pathologists respond.
- NOTE Confidence: 0.766632917142857

 $00:25:24.480 \longrightarrow 00:25:25.845$ You can see that half of them

NOTE Confidence: 0.766632917142857

00:25:25.845 --> 00:25:27.265 were from North America, roughly,

NOTE Confidence: 0.766632917142857

 $00:25:27.265 \rightarrow 00:25:29.935$ and half were roughly from Europe.

NOTE Confidence: 0.766632917142857

 $00:25:29.940 \longrightarrow 00:25:32.280$ And a wide range of.

NOTE Confidence: 0.766632917142857

 $00{:}25{:}32{.}280 \dashrightarrow 00{:}25{:}34{.}614$ Of sort of experience with heart

NOTE Confidence: 0.766632917142857

 $00{:}25{:}34{.}614 \dashrightarrow 00{:}25{:}37{.}353$ biopsies from less than 10 think a

NOTE Confidence: 0.766632917142857

 $00:25:37.353 \rightarrow 00:25:39.573$ reasonable chunk to greater than 200.

NOTE Confidence: 0.766632917142857

 $00{:}25{:}39{.}580 \dashrightarrow 00{:}25{:}43{.}136$ And I have a colleague in Germany.

NOTE Confidence: 0.766632917142857

00:25:43.140 --> 00:25:44.440 Who Karen Klingle,

NOTE Confidence: 0.766632917142857

 $00:25:44.440 \rightarrow 00:25:47.240$ who sees thousands of cases every year.

NOTE Confidence: 0.766632917142857

 $00{:}25{:}47{.}240 \dashrightarrow 00{:}25{:}48{.}446$ She I think is the referral

NOTE Confidence: 0.766632917142857

 $00:25:48.446 \longrightarrow 00:25:49.660$ Center for all of Germany.

NOTE Confidence: 0.766632917142857

 $00{:}25{:}49.660 \dashrightarrow 00{:}25{:}52.412$ So she has a huge cohort of cases and a lot

NOTE Confidence: 0.766632917142857

 $00{:}25{:}52{.}412 \dashrightarrow 00{:}25{:}54{.}876$ of experience and she participated as well.

NOTE Confidence: 0.766632917142857

 $00{:}25{:}54.880 \dashrightarrow 00{:}25{:}56.424$ So we started to ask this group questions

NOTE Confidence: 0.766632917142857

 $00:25:56.424 \rightarrow 00:25:57.919$ and the first question we asked is,

- NOTE Confidence: 0.766632917142857
- $00:25:57.920 \longrightarrow 00:26:00.335$ do we all use the same criteria?
- NOTE Confidence: 0.766632917142857
- 00:26:00.340 --> 00:26:00.696 No,
- NOTE Confidence: 0.766632917142857
- $00:26:00.696 \longrightarrow 00:26:01.408$ we don't.
- NOTE Confidence: 0.766632917142857
- $00:26:01.408 \longrightarrow 00:26:03.900$ You can see that half the people
- NOTE Confidence: 0.766632917142857
- $00{:}26{:}03.987 \dashrightarrow 00{:}26{:}06.467$ use Dallas criteria exclusively,
- NOTE Confidence: 0.766632917142857
- $00:26:06.470 \longrightarrow 00:26:07.914$ 28 used both criteria,
- NOTE Confidence: 0.766632917142857
- 00:26:07.914 --> 00:26:09.719 the European and Dallas criteria,
- NOTE Confidence: 0.766632917142857
- $00{:}26{:}09{.}720 \dashrightarrow 00{:}26{:}10{.}880$ and 12 claim to use.
- NOTE Confidence: 0.766632917142857
- $00{:}26{:}10.880 \dashrightarrow 00{:}26{:}13.568$ The European eight people didn't use either,
- NOTE Confidence: 0.766632917142857
- $00:26:13.570 \longrightarrow 00:26:15.148$ and this was somewhat dependent on
- NOTE Confidence: 0.766632917142857
- $00:26:15.148 \rightarrow 00:26:17.149$ where in the world they were located.
- NOTE Confidence: 0.766632917142857
- 00:26:17.150 --> 00:26:18.665 In North America,
- NOTE Confidence: 0.766632917142857
- $00:26:18.665 \longrightarrow 00:26:20.180$ people predominantly use
- NOTE Confidence: 0.766632917142857
- 00:26:20.180 --> 00:26:22.200 just the Dallas criteria,
- NOTE Confidence: 0.766632917142857
- $00{:}26{:}22{.}200 \dashrightarrow 00{:}26{:}24{.}366$ whereas in Europe they seem to
- NOTE Confidence: 0.766632917142857

 $00:26:24.366 \rightarrow 00:26:27.213$ mostly use your the ESC and then

NOTE Confidence: 0.766632917142857

 $00{:}26{:}27{.}213 \dashrightarrow 00{:}26{:}29{.}423$ potentially Dallas criteria as well.

NOTE Confidence: 0.766632917142857

 $00:26:29.430 \longrightarrow 00:26:31.120$ So very much depends on.

NOTE Confidence: 0.766632917142857

 $00:26:31.120 \rightarrow 00:26:33.628$ Where they were, we use criteria, no.

NOTE Confidence: 0.766632917142857

 $00:26:33.628 \rightarrow 00:26:35.182$ What about immunohistochemistry

NOTE Confidence: 0.766632917142857

 $00:26:35.182 \longrightarrow 00:26:37.254$ and viral PCR studies?

NOTE Confidence: 0.766632917142857

00:26:37.260 --> 00:26:39.500 Do we use these consistently?

NOTE Confidence: 0.766632917142857

 $00:26:39.500 \rightarrow 00:26:39.980$ No.

NOTE Confidence: 0.766632917142857

00:26:39.980 --> 00:26:40.460 OK,

NOTE Confidence: 0.766632917142857

 $00:26:40.460 \longrightarrow 00:26:41.900$ on the left,

NOTE Confidence: 0.766632917142857

 $00{:}26{:}41{.}900 \dashrightarrow 00{:}26{:}43{.}364$ you see that half the European

NOTE Confidence: 0.766632917142857

 $00:26:43.364 \rightarrow 00:26:44.959$ groups use IHC in every case,

NOTE Confidence: 0.766632917142857

 $00:26:44.960 \rightarrow 00:26:47.975$ and the other group do it in selected cases.

NOTE Confidence: 0.766632917142857

 $00:26:47.980 \longrightarrow 00:26:49.820$ And in the United States,

NOTE Confidence: 0.766632917142857

 $00:26:49.820 \longrightarrow 00:26:52.226$ there's a group that do not

NOTE Confidence: 0.766632917142857

 $00:26:52.226 \rightarrow 00:26:53.028$ perform immunohistochemistry

- NOTE Confidence: 0.766632917142857
- $00:26:53.028 \longrightarrow 00:26:55.299$ on any cases for myocarditis.

00:26:55.300 --> 00:26:57.113 And I will tell you that my

NOTE Confidence: 0.766632917142857

00:26:57.113 -> 00:26:58.639 colleagues at the Mayo Clinic,

NOTE Confidence: 0.766632917142857

 $00{:}26{:}58{.}640 \dashrightarrow 00{:}27{:}00{.}292$ who are some of the best cardiovascular

NOTE Confidence: 0.766632917142857

00:27:00.292 --> 00:27:01.360 pathologists in the country,

NOTE Confidence: 0.766632917142857

 $00:27:01.360 \rightarrow 00:27:03.024$ don't use immunohistochemistry because

NOTE Confidence: 0.766632917142857

 $00:27:03.024 \rightarrow 00:27:06.160$ it's not part of the Dallas criteria.

NOTE Confidence: 0.766632917142857

 $00{:}27{:}06.160 \dashrightarrow 00{:}27{:}08.195$ I'll mention before that sometimes

NOTE Confidence: 0.766632917142857

 $00{:}27{:}08.195 \dashrightarrow 00{:}27{:}11.220$ people use viral PCR to type viruses.

NOTE Confidence: 0.766632917142857

 $00:27:11.220 \longrightarrow 00:27:12.640$ Some people consider that an

NOTE Confidence: 0.766632917142857

00:27:12.640 --> 00:27:14.060 important part of the diagnosis,

NOTE Confidence: 0.766632917142857

 $00{:}27{:}14.060 \dashrightarrow 00{:}27{:}15.192$ other people do not.

NOTE Confidence: 0.766632917142857

00:27:15.192 --> 00:27:15.758 In Europe,

NOTE Confidence: 0.834491297142857

 $00{:}27{:}15.760 \dashrightarrow 00{:}27{:}18.119$ about half the groups routinely perform it,

NOTE Confidence: 0.834491297142857

 $00:27:18.120 \longrightarrow 00:27:20.720$ and North America's only 22%.

 $00:27:20.720 \rightarrow 00:27:22.730$ At my institution, the pediatric team

NOTE Confidence: 0.834491297142857

 $00{:}27{:}22.730 \dashrightarrow 00{:}27{:}24.958$ performs it and the adults do not.

NOTE Confidence: 0.834491297142857

00:27:24.960 --> 00:27:28.467 So even in one institution we have

NOTE Confidence: 0.834491297142857

 $00:27:28.467 \rightarrow 00:27:31.009$ different approaches to doing this.

NOTE Confidence: 0.834491297142857

 $00{:}27{:}31.010 \dashrightarrow 00{:}27{:}33.234$ Well, do we use the same terminology to

NOTE Confidence: 0.834491297142857

 $00{:}27{:}33{.}234 \dashrightarrow 00{:}27{:}35{.}730$ all of us use at least the same terms?

NOTE Confidence: 0.834491297142857

00:27:35.730 --> 00:27:38.970 Again, no. You can see that giant cell

NOTE Confidence: 0.834491297142857

 $00:27:38.970 \rightarrow 00:27:41.240$ myocarditis was the most commonly used

NOTE Confidence: 0.834491297142857

 $00:27:41.240 \longrightarrow 00:27:44.140$ term as like a top line diagnosis,

NOTE Confidence: 0.834491297142857

00:27:44.140 --> 00:27:45.832 you syphilitic myocarditis,

NOTE Confidence: 0.834491297142857

 $00{:}27{:}45.832 \dashrightarrow 00{:}27{:}48.088$ lymphocytic myocarditis and down.

NOTE Confidence: 0.834491297142857

 $00:27:48.090 \longrightarrow 00:27:50.415$ But note that borderline myocarditis

NOTE Confidence: 0.834491297142857

 $00{:}27{:}50{.}415 \dashrightarrow 00{:}27{:}53{.}662$ was used by 55% of the group.

NOTE Confidence: 0.834491297142857

 $00{:}27{:}53.662 \dashrightarrow 00{:}27{:}55.514$ So that intermediate diagnosis

NOTE Confidence: 0.834491297142857

 $00:27:55.514 \rightarrow 00:27:57.829$ wasn't even used by everyone.

NOTE Confidence: 0.834491297142857

 $00:27:57.830 \rightarrow 00:28:01.993$ So this might be concerning, I don't know.

- NOTE Confidence: 0.834491297142857
- $00{:}28{:}01{.}993 \dashrightarrow 00{:}28{:}03{.}919$ Our conclusions were that there is
- NOTE Confidence: 0.834491297142857
- $00{:}28{:}03{.}919$ --> $00{:}28{:}06{.}338$ not a consistent approach and the way
- NOTE Confidence: 0.834491297142857
- $00:28:06.338 \rightarrow 00:28:08.689$ we make the diagnosis of myocarditis,
- NOTE Confidence: 0.834491297142857
- $00:28:08.690 \longrightarrow 00:28:10.362$ we have different criteria,
- NOTE Confidence: 0.834491297142857
- $00:28:10.362 \longrightarrow 00:28:12.452$ we have different use of
- NOTE Confidence: 0.834491297142857
- 00:28:12.452 --> 00:28:12.870 immunohistochemistry,
- NOTE Confidence: 0.834491297142857
- $00{:}28{:}12.870 \dashrightarrow 00{:}28{:}15.089$ different use of viral PCR and other
- NOTE Confidence: 0.834491297142857
- $00:28:15.089 \rightarrow 00:28:17.831$ things which I didn't bring up here, but.
- NOTE Confidence: 0.834491297142857
- 00:28:17.831 --> 00:28:19.936 But maybe there's good news.
- NOTE Confidence: 0.834491297142857
- 00:28:19.940 --> 00:28:21.596 What if it doesn't matter how
- NOTE Confidence: 0.834491297142857
- $00:28:21.596 \longrightarrow 00:28:23.410$ we get to the diagnosis,
- NOTE Confidence: 0.834491297142857
- $00:28:23.410 \longrightarrow 00:28:25.466$ it's so obvious that we all get to
- NOTE Confidence: 0.834491297142857
- $00{:}28{:}25{.}466 \dashrightarrow 00{:}28{:}27{.}540$ the same diagnosis no matter what.
- NOTE Confidence: 0.834491297142857
- $00{:}28{:}27{.}540 \dashrightarrow 00{:}28{:}30{.}836$ OK, so may be this is like, you know,
- NOTE Confidence: 0.834491297142857
- $00:28:30.836 \rightarrow 00:28:32.076$ trying to thin slice something
- NOTE Confidence: 0.834491297142857

 $00:28:32.076 \rightarrow 00:28:33.160$ that doesn't really matter.

NOTE Confidence: 0.834491297142857

00:28:33.160 --> 00:28:34.275 We're going to anyone doesn't

NOTE Confidence: 0.834491297142857

00:28:34.275 --> 00:28:35.593 matter what criteria they use are

NOTE Confidence: 0.834491297142857

 $00:28:35.593 \rightarrow 00:28:36.720$ going to see the slide and go,

NOTE Confidence: 0.834491297142857

 $00:28:36.720 \longrightarrow 00:28:37.262$ that's myocarditis.

NOTE Confidence: 0.834491297142857

 $00{:}28{:}37{.}262 \dashrightarrow 00{:}28{:}38{.}617$ We're all going to agree.

NOTE Confidence: 0.834491297142857

 $00:28:38.620 \longrightarrow 00:28:39.556$ That's not myocarditis.

NOTE Confidence: 0.834491297142857

00:28:39.556 --> 00:28:41.428 We're all gonna agree and that

NOTE Confidence: 0.834491297142857

 $00:28:41.428 \longrightarrow 00:28:42.260$ would be great.

NOTE Confidence: 0.834491297142857

00:28:42.260 --> 00:28:44.648 So wouldn't a bunch of experts

NOTE Confidence: 0.834491297142857

 $00:28:44.648 \longrightarrow 00:28:47.569$ all agree on what is myocarditis?

NOTE Confidence: 0.834491297142857

 $00{:}28{:}47.570 \dashrightarrow 00{:}28{:}49.866$ And so we did that experiment as well.

NOTE Confidence: 0.834491297142857

 $00{:}28{:}49{.}870 \dashrightarrow 00{:}28{:}52{.}633$ Here I had the pleasure

NOTE Confidence: 0.834491297142857

 $00:28:52.633 \longrightarrow 00:28:53.748$ of working with Dan Liu,

NOTE Confidence: 0.834491297142857

 $00{:}28{:}53.750 \dashrightarrow 00{:}28{:}55.574$ one of our trainees at Johns

NOTE Confidence: 0.834491297142857

 $00:28:55.574 \rightarrow 00:28:57.429$ Hopkins where he blessed his heart,

00:28:57.430 --> 00:28:59.655 digitized 100 heart biopsy cases

NOTE Confidence: 0.834491297142857

 $00{:}28{:}59{.}655 \dashrightarrow 00{:}29{:}02{.}670$ on a slick 6 slide scanner.

NOTE Confidence: 0.834491297142857

 $00{:}29{:}02{.}670 \dashrightarrow 00{:}29{:}04{.}536$ These are diagnosis of cases that

NOTE Confidence: 0.834491297142857

 $00:29:04.536 \rightarrow 00:29:06.668$ either myself or my colleague Charles

NOTE Confidence: 0.834491297142857

00:29:06.668 --> 00:29:09.134 Steenbergen had made at Johns Hopkins,

NOTE Confidence: 0.834491297142857

 $00{:}29{:}09{.}140 \dashrightarrow 00{:}29{:}12{.}180$ 31 cases of myocarditis 32 that we had

NOTE Confidence: 0.834491297142857

00:29:12.180 --> 00:29:14.730 diagnosed as borderline myocarditis,

NOTE Confidence: 0.834491297142857

 $00:29:14.730 \longrightarrow 00:29:17.700$ 37 cases of non myocarditis.

NOTE Confidence: 0.834491297142857

00:29:17.700 --> 00:29:22.355 All cases had H&E's, usually four slides,

NOTE Confidence: 0.834491297142857

00:29:22.360 --> 00:29:23.740 CD3, CD 68 and a Mason,

NOTE Confidence: 0.834491297142857

00:29:23.740 --> 00:29:24.095 trichrome,

NOTE Confidence: 0.834491297142857

 $00{:}29{:}24.095 \dashrightarrow 00{:}29{:}26.580$ that were all scanned and made available.

NOTE Confidence: 0.834491297142857

 $00{:}29{:}26.580 \dashrightarrow 00{:}29{:}29.135$ We had a panel of eight international

NOTE Confidence: 0.834491297142857

 $00:29:29.135 \rightarrow 00:29:31.604$ experts who were invited to independently

NOTE Confidence: 0.834491297142857

 $00{:}29{:}31.604 \dashrightarrow 00{:}29{:}34.214$ provide a diagnosis on each case.

 $00:29:34.220 \rightarrow 00:29:36.166$ They basically use the system I used

NOTE Confidence: 0.834491297142857

 $00:29:36.166 \rightarrow 00:29:38.140$ this morning with the trainees proscia,

NOTE Confidence: 0.834491297142857

 $00{:}29{:}38.140 \dashrightarrow 00{:}29{:}40.576$ just digital slides with a scoring sheet.

NOTE Confidence: 0.834491297142857

 $00:29:40.580 \longrightarrow 00:29:42.360$ The cases were all randomized.

NOTE Confidence: 0.834491297142857

 $00{:}29{:}42{.}360 \dashrightarrow 00{:}29{:}44{.}712$ We told them only that every body had

NOTE Confidence: 0.834491297142857

 $00{:}29{:}44.712 \dashrightarrow 00{:}29{:}47.179$ a diagnosis of rule out myocarditis.

NOTE Confidence: 0.834491297142857

 $00{:}29{:}47.180 \dashrightarrow 00{:}29{:}48.780$ Our plan was that they would have a

NOTE Confidence: 0.834491297142857

 $00:29:48.780 \rightarrow 00:29:50.540$ lot of agreement where they didn't

NOTE Confidence: 0.834491297142857

 $00:29:50.540 \rightarrow 00:29:52.180$ have agreement between the groups.

NOTE Confidence: 0.834491297142857

 $00:29:52.180 \rightarrow 00:29:54.140$ We would resolve this maybe by e-mail.

NOTE Confidence: 0.834491297142857

 $00:29:54.140 \longrightarrow 00:29:55.514$ So let's say seven of eight

NOTE Confidence: 0.834491297142857

 $00:29:55.514 \rightarrow 00:29:57.080$ agreed that it was myocarditis.

NOTE Confidence: 0.834491297142857

00:29:57.080 --> 00:29:58.556 One person said borderline would say,

NOTE Confidence: 0.834491297142857

 $00:29:58.560 \rightarrow 00:30:00.900$ hey, everyone else is saying myocarditis.

NOTE Confidence: 0.834491297142857

 $00:30:00.900 \longrightarrow 00:30:02.348$ What do you think?

NOTE Confidence: 0.834491297142857

 $00:30:02.348 \longrightarrow 00:30:04.940$ If they said OK, we would say that's great.

00:30:04.940 --> 00:30:07.136 If they say, Nope, I'm sticking to my guns,

NOTE Confidence: 0.834491297142857

 $00:30:07.140 \longrightarrow 00:30:08.204$ we say, that's fine,

NOTE Confidence: 0.834491297142857

 $00{:}30{:}08{.}204 \dashrightarrow 00{:}30{:}09{.}800$ we'll have a shared zoom session

NOTE Confidence: 0.834491297142857

 $00{:}30{:}09{.}854 \dashrightarrow 00{:}30{:}11{.}541$ and we'll talk about all the cases

NOTE Confidence: 0.834491297142857

 $00:30:11.541 \longrightarrow 00:30:13.070$ that we don't have agreement.

NOTE Confidence: 0.834491297142857

 $00{:}30{:}13.070 \dashrightarrow 00{:}30{:}15.345$ So 100 cases, it should be great.

NOTE Confidence: 0.85244914

 $00:30:15.350 \rightarrow 00:30:17.430$ Nothing could go wrong.

NOTE Confidence: 0.85244914

 $00:30:17.430 \longrightarrow 00:30:20.104$ Well, it turned out that getting to

NOTE Confidence: 0.85244914

 $00:30:20.104 \dashrightarrow 00:30:22.548$ consensus was really challenging to me.

NOTE Confidence: 0.85244914

00:30:22.550 --> 00:30:23.132 Surprisingly challenging.

NOTE Confidence: 0.85244914

 $00{:}30{:}23{.}132 \dashrightarrow 00{:}30{:}25{.}460$ Although when I told the colleague he's like,

NOTE Confidence: 0.85244914

 $00:30:25.460 \rightarrow 00:30:27.444$ why are you thinking this would be easy?

NOTE Confidence: 0.85244914

00:30:27.450 --> 00:30:28.443 I don't know.

NOTE Confidence: 0.85244914

 $00{:}30{:}28{.}443 \dashrightarrow 00{:}30{:}31{.}291$ So this is the initial consensus to the

NOTE Confidence: 0.85244914

 $00{:}30{:}31{.}291 \dashrightarrow 00{:}30{:}34{.}069$ Johns Hopkins signed out original diagnosis.

 $00:30:34.070 \longrightarrow 00:30:35.718$ They had full consensus.

NOTE Confidence: 0.85244914

00:30:35.718 --> 00:30:38.675 All eight people agreed on the on

NOTE Confidence: 0.85244914

 $00{:}30{:}38.675 \dashrightarrow 00{:}30{:}40.850$ the diagnosis of borderline cases.

NOTE Confidence: 0.85244914

00:30:40.850 --> 00:30:44.516 Three 3 * 16 agreed on

NOTE Confidence: 0.85244914

 $00:30:44.516 \longrightarrow 00:30:48.010$ myocarditis cases 18 all agreed.

NOTE Confidence: 0.85244914

00:30:48.010 --> 00:30:49.306 On non myocarditis cases and I

NOTE Confidence: 0.85244914

00:30:49.306 --> 00:30:50.914 should go back for a moment and

NOTE Confidence: 0.85244914

 $00:30:50.914 \rightarrow 00:30:52.300$ say for the non myocarditis cases,

NOTE Confidence: 0.85244914

 $00{:}30{:}52{.}300 \dashrightarrow 00{:}30{:}53{.}715$ I was specifically looking for

NOTE Confidence: 0.85244914

 $00{:}30{:}53.715 \dashrightarrow 00{:}30{:}55.549$ ones that I had reported as

NOTE Confidence: 0.85244914

 $00{:}30{:}55{.}549 \dashrightarrow 00{:}30{:}57{.}374$ having a little more inflammatory

NOTE Confidence: 0.85244914

 $00:30:57.374 \rightarrow 00:30:58.834$ infiltrate than complete baseline.

NOTE Confidence: 0.85244914

 $00:30:58.840 \longrightarrow 00:31:01.724$ So it made it a little harder.

NOTE Confidence: 0.85244914

 $00:31:01.730 \longrightarrow 00:31:04.285$ You see, for the three borderline cases,

NOTE Confidence: 0.85244914

 $00{:}31{:}04.290 \dashrightarrow 00{:}31{:}05.542$ while they all agreed,

NOTE Confidence: 0.85244914

 $00:31:05.542 \rightarrow 00:31:07.107$ they didn't agree with me,

- NOTE Confidence: 0.85244914
- $00:31:07.110 \rightarrow 00:31:08.688$ all these people, those three cases,

 $00{:}31{:}08.690 \dashrightarrow 00{:}31{:}10.790$ every one said this is not myocarditis.

NOTE Confidence: 0.85244914

00:31:10.790 --> 00:31:12.110 So they're basically saying, sorry,

NOTE Confidence: 0.85244914

00:31:12.110 --> 00:31:13.830 Mark, you blew that diagnosis,

NOTE Confidence: 0.85244914

00:31:13.830 --> 00:31:14.994 OK, that's fine.

NOTE Confidence: 0.85244914

 $00{:}31{:}14.994 \dashrightarrow 00{:}31{:}17.710$ We had moderate diagnosis then on 13,

NOTE Confidence: 0.85244914

 $00{:}31{:}17{.}710 \dashrightarrow 00{:}31{:}20{.}702$ nine and 13 cases where this was at

NOTE Confidence: 0.85244914

 $00{:}31{:}20.702 \dashrightarrow 00{:}31{:}23.947$ least six of the eight people agreeing.

NOTE Confidence: 0.85244914

 $00:31:23.950 \longrightarrow 00:31:25.987$ And then we had 28 cases overall

NOTE Confidence: 0.85244914

 $00:31:25.987 \rightarrow 00:31:27.769$ where there was low agreement.

NOTE Confidence: 0.85244914

 $00{:}31{:}27.770 \dashrightarrow 00{:}31{:}30.269$ We had some cases where people said

NOTE Confidence: 0.85244914

 $00{:}31{:}30{.}269 \dashrightarrow 00{:}31{:}32{.}409$ non myocarditis, some people said.

NOTE Confidence: 0.85244914

 $00{:}31{:}32{.}409 \dashrightarrow 00{:}31{:}35{.}247$ Borderline markers and other people said

NOTE Confidence: 0.85244914

 $00{:}31{:}35{.}247 \dashrightarrow 00{:}31{:}37{.}349$ myocarditis all on the same slides.

NOTE Confidence: 0.85244914

 $00{:}31{:}37{.}350 \dashrightarrow 00{:}31{:}39{.}166$ And that was interesting.

- $00:31:39.166 \rightarrow 00:31:40.789$ So we said, OK,
- NOTE Confidence: 0.85244914
- $00:31:40.789 \longrightarrow 00:31:41.048$ we,
- NOTE Confidence: 0.85244914
- $00{:}31{:}41.048 \dashrightarrow 00{:}31{:}43.120$ we worked through this and we had a
- NOTE Confidence: 0.85244914
- $00:31:43.185 \rightarrow 00:31:45.292$ couple of big zoom sessions where we
- NOTE Confidence: 0.85244914
- $00:31:45.292 \longrightarrow 00:31:47.528$ got people to try and work on this.
- NOTE Confidence: 0.85244914
- $00:31:47.530 \longrightarrow 00:31:49.906$ It didn't get that much better.
- NOTE Confidence: 0.85244914
- 00:31:49.910 --> 00:31:50.219 First,
- NOTE Confidence: 0.85244914
- $00:31:50.219 \rightarrow 00:31:52.691$ I discovered that two of my experts don't
- NOTE Confidence: 0.85244914
- $00{:}31{:}52.691 \dashrightarrow 00{:}31{:}55.029$ use the intermediate borderline term.
- NOTE Confidence: 0.85244914
- $00:31:55.030 \rightarrow 00:31:57.704$ So they were refusing to use the
- NOTE Confidence: 0.85244914
- 00:31:57.704 > 00:31:58.850 term borderline myocarditis.
- NOTE Confidence: 0.85244914
- $00:31:58.850 \longrightarrow 00:32:00.698$ Now at least one of them had an
- NOTE Confidence: 0.85244914
- $00:32:00.698 \rightarrow 00:32:02.147$ intermediate term that they would use,
- NOTE Confidence: 0.85244914
- $00:32:02.150 \longrightarrow 00:32:03.910$ which was like myocardium
- NOTE Confidence: 0.85244914
- $00{:}32{:}03{.}910$ --> $00{:}32{:}05{.}230$ with increased inflammation.
- NOTE Confidence: 0.85244914
- 00:32:05.230 --> 00:32:06.210 And I'd say, well,

- NOTE Confidence: 0.85244914
- $00:32:06.210 \longrightarrow 00:32:07.680$ can't you just call that borderline?

00:32:07.680 --> 00:32:08.069 No,

NOTE Confidence: 0.85244914

 $00:32:08.069 \longrightarrow 00:32:10.014$ my clinicians like either yes

NOTE Confidence: 0.85244914

 $00:32:10.014 \rightarrow 00:32:12.519$ or no for making the diagnosis

NOTE Confidence: 0.85244914

00:32:12.519 -> 00:32:14.694 of myocarditis and they're happy

NOTE Confidence: 0.85244914

 $00:32:14.694 \longrightarrow 00:32:17.718$ to try to please the clinician.

NOTE Confidence: 0.85244914

 $00:32:17.720 \longrightarrow 00:32:20.440$ We had 10 cases that were mostly borderline,

NOTE Confidence: 0.85244914

 $00{:}32{:}20{.}440 \dashrightarrow 00{:}32{:}22{.}060$ which we achieved no consensus.

NOTE Confidence: 0.85244914

 $00{:}32{:}22.060 \dashrightarrow 00{:}32{:}24.076$ We we sat around and talked about

NOTE Confidence: 0.85244914

 $00:32:24.076 \longrightarrow 00:32:26.071$ them and couldn't get everybody to

NOTE Confidence: 0.85244914

 $00:32:26.071 \rightarrow 00:32:28.207$ agree whether it was borderline or

NOTE Confidence: 0.85244914

 $00{:}32{:}28.207 \dashrightarrow 00{:}32{:}30.037$ myocarditis or borderline or nothing.

NOTE Confidence: 0.85244914

 $00:32:30.040 \longrightarrow 00:32:31.876$ And we we just dropped those

NOTE Confidence: 0.85244914

 $00{:}32{:}31.876 \dashrightarrow 00{:}32{:}33.100$ cases and moved on.

NOTE Confidence: 0.85244914

 $00:32:33.100 \rightarrow 00:32:36.412$ And then we had one case of borderline Plus,

 $00:32:36.420 \longrightarrow 00:32:38.576$ which is not even a real term.

NOTE Confidence: 0.85244914

00:32:38.580 --> 00:32:39.932 We just invented it so we could get

NOTE Confidence: 0.85244914

 $00{:}32{:}39{.}932 \dashrightarrow 00{:}32{:}41{.}548$ to a consensus because everyone agreed

NOTE Confidence: 0.85244914

 $00:32:41.548 \longrightarrow 00:32:43.093$ to calling this borderline plus.

NOTE Confidence: 0.85244914

 $00:32:43.100 \longrightarrow 00:32:45.424$ But this is the Histology of that

NOTE Confidence: 0.85244914

 $00:32:45.424 \rightarrow 00:32:47.940$ case and you can kind of see why.

NOTE Confidence: 0.85244914

00:32:47.940 --> 00:32:49.077 This was challenging.

NOTE Confidence: 0.85244914

 $00:32:49.077 \rightarrow 00:32:51.730$ We had clearly collections of immune cells,

NOTE Confidence: 0.85244914

 $00:32:51.730 \longrightarrow 00:32:52.579$ way too many,

NOTE Confidence: 0.85244914

 $00:32:52.579 \rightarrow 00:32:54.560$ although they are on the surface here

NOTE Confidence: 0.85244914

 $00{:}32{:}54{.}623 \dashrightarrow 00{:}32{:}56{.}423$ we had collections that were inside

NOTE Confidence: 0.85244914

 $00:32:56.423 \rightarrow 00:32:58.350$ the tissue of many lymphocytes.

NOTE Confidence: 0.85244914

 $00:32:58.350 \rightarrow 00:33:00.846$ Here's a collection by CD3 and

NOTE Confidence: 0.85244914

 $00:33:00.846 \longrightarrow 00:33:02.510$ another collection of CD3.

NOTE Confidence: 0.85244914

 $00{:}33{:}02{.}510 \dashrightarrow 00{:}33{:}04{.}946$ So clearly lots and lots of cells.

NOTE Confidence: 0.85244914

00:33:04.950 - 00:33:07.194 Some people wanted to call this

- NOTE Confidence: 0.85244914
- 00:33:07.194 --> 00:33:08.690 myocarditis even without injury
- NOTE Confidence: 0.85244914
- $00{:}33{:}08.757 \dashrightarrow 00{:}33{:}10.815$ and some people just wanted to
- NOTE Confidence: 0.85244914
- $00:33:10.815 \longrightarrow 00:33:11.844$ call this borderline.
- NOTE Confidence: 0.890533379583333
- $00{:}33{:}11.850 \dashrightarrow 00{:}33{:}13.074$ So all of this.
- NOTE Confidence: 0.890533379583333
- $00{:}33{:}13.074 \dashrightarrow 00{:}33{:}15.802$ Was a bit of a problem because even
- NOTE Confidence: 0.890533379583333
- $00:33:15.802 \rightarrow 00:33:18.623$ my experts don't agree on how to
- NOTE Confidence: 0.890533379583333
- $00:33:18.623 \rightarrow 00:33:21.447$ make the diagnosis of myocarditis.
- NOTE Confidence: 0.890533379583333
- $00:33:21.450 \longrightarrow 00:33:23.274$ So to kind of sum all this up,
- NOTE Confidence: 0.890533379583333
- $00:33:23.280 \longrightarrow 00:33:24.948$ we really have challenges
- NOTE Confidence: 0.890533379583333
- $00:33:24.948 \longrightarrow 00:33:27.033$ in the world of myocarditis.
- NOTE Confidence: 0.890533379583333
- 00:33:27.040 --> 00:33:28.692 Cardiac MRI is good,
- NOTE Confidence: 0.890533379583333
- 00:33:28.692 --> 00:33:30.757 but is not necessarily robust
- NOTE Confidence: 0.890533379583333
- $00:33:30.757 \longrightarrow 00:33:33.039$ in all clinical scenarios.
- NOTE Confidence: 0.890533379583333
- $00{:}33{:}33{.}040 \dashrightarrow 00{:}33{:}35{.}050$ There are no specific clinical
- NOTE Confidence: 0.890533379583333
- 00:33:35.050 00:33:37.060 symptoms or lab findings that
- NOTE Confidence: 0.890533379583333

00:33:37.134 --> 00:33:39.078 are specific for myocarditis.

NOTE Confidence: 0.890533379583333

00:33:39.080 --> 00:33:40.332 The micronite biomarker that

NOTE Confidence: 0.890533379583333

00:33:40.332 --> 00:33:42.500 was claimed is not a micro RNA,

NOTE Confidence: 0.890533379583333

00:33:42.500 - 00:33:44.350 probably to definitely not a

NOTE Confidence: 0.890533379583333

 $00:33:44.350 \longrightarrow 00:33:46.678$ biomarker one in 2.5 billion chance.

NOTE Confidence: 0.890533379583333

 $00:33:46.678 \rightarrow 00:33:49.114$ Not all pathologists use the same

NOTE Confidence: 0.890533379583333

 $00{:}33{:}49{.}114 \dashrightarrow 00{:}33{:}51{.}135$ criteria to make the diagnosis

NOTE Confidence: 0.890533379583333

 $00{:}33{:}51{.}135 \dashrightarrow 00{:}33{:}53{.}065$ of myocarditis and even experts

NOTE Confidence: 0.890533379583333

00:33:53.065 --> 00:33:55.229 don't agree on diagnosing cases,

NOTE Confidence: 0.890533379583333

 $00:33:55.230 \rightarrow 00:33:59.070$ particularly the intermediate grade lesions.

NOTE Confidence: 0.890533379583333

00:33:59.070 - 00:34:01.250 But where there are challenges,

NOTE Confidence: 0.890533379583333

 $00:34:01.250 \longrightarrow 00:34:02.450$ there are opportunities.

NOTE Confidence: 0.890533379583333

 $00:34:02.450 \longrightarrow 00:34:05.710$ So what can we do to improve this?

NOTE Confidence: 0.890533379583333

 $00{:}34{:}05{.}710 \dashrightarrow 00{:}34{:}07{.}564$ The first thing we want to do is try

NOTE Confidence: 0.890533379583333

 $00:34:07.564 \rightarrow 00:34:09.586$ and get the diagnostic criteria right.

NOTE Confidence: 0.890533379583333

 $00:34:09.590 \rightarrow 00:34:12.368$ Can we improve the Dallas criteria?

 $00{:}34{:}12{.}370 \dashrightarrow 00{:}34{:}14{.}826$ And the 2nd is to develop better tissue

NOTE Confidence: 0.890533379583333

 $00:34:14.826 \rightarrow 00:34:16.898$ based methods to diagnose myocarditis.

NOTE Confidence: 0.890533379583333

 $00:34:16.900 \rightarrow 00:34:19.040$ So those are going to be the last two parts.

NOTE Confidence: 0.890533379583333

 $00:34:19.040 \rightarrow 00:34:21.695$ Of the talk and the first part is going

NOTE Confidence: 0.890533379583333

 $00{:}34{:}21.695 \dashrightarrow 00{:}34{:}24.317$ to be revising the Dallas criteria.

NOTE Confidence: 0.890533379583333

 $00:34:24.320 \longrightarrow 00:34:26.336$ So let's talk about some opportunities

NOTE Confidence: 0.890533379583333

 $00:34:26.336 \longrightarrow 00:34:28.240$ to improve the Dallas criteria.

NOTE Confidence: 0.890533379583333

00:34:28.240 --> 00:34:29.736 We can incorporate immunohistochemistry,

NOTE Confidence: 0.890533379583333

 $00:34:29.736 \longrightarrow 00:34:32.560$ which is not part of the original.

NOTE Confidence: 0.890533379583333

 $00:34:32.560 \rightarrow 00:34:34.678$ We can better define myocyte injury

NOTE Confidence: 0.890533379583333

 $00:34:34.678 \rightarrow 00:34:37.123$ as very nebulous and the original

NOTE Confidence: 0.890533379583333

 $00:34:37.123 \dashrightarrow 00:34:39.055$ diagnosis open to interpretation.

NOTE Confidence: 0.890533379583333

 $00{:}34{:}39{.}060 \dashrightarrow 00{:}34{:}41{.}538$ We can improve thresholds for immune cells.

NOTE Confidence: 0.890533379583333

 $00:34:41.540 \longrightarrow 00:34:43.878$ How many cells is it to say

NOTE Confidence: 0.890533379583333

 $00:34:43.878 \rightarrow 00:34:44.880$ this is borderline?

 $00:34:44.880 \rightarrow 00:34:47.835$ How many is it say this is too many to be

NOTE Confidence: 0.890533379583333

 $00:34:47.835 \rightarrow 00:34:50.439$ in some intermediate category or categories?

NOTE Confidence: 0.890533379583333

 $00:34:50.440 \dashrightarrow 00:34:53.499$ Validate terms and diagnosis to outcome data.

NOTE Confidence: 0.890533379583333

 $00:34:53.500 \rightarrow 00:34:55.460$ I think that's going to be important

NOTE Confidence: 0.890533379583333

 $00{:}34{:}55{.}460 \dashrightarrow 00{:}34{:}57{.}465$ to show that these are meaningful

NOTE Confidence: 0.890533379583333

 $00{:}34{:}57{.}465 \dashrightarrow 00{:}35{:}00{.}027$ descriptors that we're using and a separate

NOTE Confidence: 0.890533379583333

00:35:00.093 --> 00:35:02.098 diagnosis on biopsies from autopsy,

NOTE Confidence: 0.890533379583333

 $00:35:02.100 \longrightarrow 00:35:02.966$ explanted hearts.

NOTE Confidence: 0.890533379583333

00:35:02.966 --> 00:35:03.399 Again,

NOTE Confidence: 0.890533379583333

 $00:35:03.399 \rightarrow 00:35:05.997$ Dallas criteria were designed for biopsies,

NOTE Confidence: 0.890533379583333

 $00:35:06.000 \dashrightarrow 00:35:08.118$ but people have been using them

NOTE Confidence: 0.890533379583333

 $00{:}35{:}08.118 \dashrightarrow 00{:}35{:}09.530$ incorrectly on autopsy hearts

NOTE Confidence: 0.890533379583333

00:35:09.593 --> 00:35:11.097 or maybe explanted hearts.

NOTE Confidence: 0.890533379583333

 $00:35:11.100 \rightarrow 00:35:15.140$ Can we use terms or develop terms and

NOTE Confidence: 0.890533379583333

 $00:35:15.140 \rightarrow 00:35:17.958$ criteria specifically for those specimens?

NOTE Confidence: 0.890533379583333

 $00:35:17.960 \longrightarrow 00:35:20.440$ So one of the things that I like

- NOTE Confidence: 0.890533379583333
- 00:35:20.440 --> 00:35:22.508 to point out is back in 1986,
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}22.508 \dashrightarrow 00{:}35{:}24.972$ it was a lot of experts sitting around
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}24{.}972 \dashrightarrow 00{:}35{:}26{.}843$ looking at slides and didn't have a
- NOTE Confidence: 0.890533379583333
- $00:35:26.843 \dashrightarrow 00:35:29.268$ lot of data to base these criteria on.
- NOTE Confidence: 0.890533379583333
- $00:35:29.270 \longrightarrow 00:35:30.838$ And we have a lot more data now.
- NOTE Confidence: 0.890533379583333
- $00:35:30.840 \longrightarrow 00:35:32.740$ People have been talking about
- NOTE Confidence: 0.890533379583333
- $00:35:32.740 \longrightarrow 00:35:34.260$ biopsies and evaluating biopsies
- NOTE Confidence: 0.890533379583333
- $00:35:34.260 \dashrightarrow 00:35:36.230$ and and reporting outcome data.
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}36{.}230 \dashrightarrow 00{:}35{:}37{.}928$ And these are two examples that
- NOTE Confidence: 0.890533379583333
- $00:35:37.928 \rightarrow 00:35:39.098$ came out in 2022,
- NOTE Confidence: 0.890533379583333
- 00:35:39.098 --> 00:35:41.006 which I think are really useful
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}41.006 \dashrightarrow 00{:}35{:}41.960$ to think about.
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}41{.}960 \dashrightarrow 00{:}35{:}45{.}306$ So this group in Spain had a
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}45{.}306 \dashrightarrow 00{:}35{:}47{.}466$ paper that looked at biopsies.
- NOTE Confidence: 0.890533379583333
- $00{:}35{:}47.466 \dashrightarrow 00{:}35{:}50.308$ With a composite end event of heart
- NOTE Confidence: 0.890533379583333

 $00:35:50.308 \longrightarrow 00:35:51.927$ transplant left ventricular assist

NOTE Confidence: 0.890533379583333

 $00{:}35{:}51{.}927 \dashrightarrow 00{:}35{:}54{.}489$ device or death and so those are

NOTE Confidence: 0.890533379583333

 $00:35:54.489 \longrightarrow 00:35:56.849$ the two things panels on the left

NOTE Confidence: 0.890533379583333

 $00:35:56.849 \rightarrow 00:35:59.429$ side here and this dark purple area.

NOTE Confidence: 0.890533379583333

 $00{:}35{:}59{.}429 \dashrightarrow 00{:}36{:}02{.}027$ Those are individuals who are Dallas

NOTE Confidence: 0.890533379583333

 $00{:}36{:}02{.}027 \dashrightarrow 00{:}36{:}04{.}531$ criteria positive and the blue is

NOTE Confidence: 0.890533379583333

 $00{:}36{:}04{.}531 \dashrightarrow 00{:}36{:}06{.}526$ Dallas criteria negative and that

NOTE Confidence: 0.890533379583333

 $00:36:06.597 \longrightarrow 00:36:09.434$ added up to the 23% or so here.

NOTE Confidence: 0.890533379583333

 $00{:}36{:}09{.}434 \dashrightarrow 00{:}36{:}12{.}140$ This is Dallas criteria negative or

NOTE Confidence: 0.890533379583333

 $00{:}36{:}12.231 \dashrightarrow 00{:}36{:}16.119$ and or sorry Dallas positive and

NOTE Confidence: 0.890533379583333

 $00{:}36{:}16.119 \dashrightarrow 00{:}36{:}18.063$ or immunohistochemistry positive.

NOTE Confidence: 0.890533379583333

00:36:18.070 --> 00:36:19.960 Suggesting that immune cells more

NOTE Confidence: 0.890533379583333

 $00{:}36{:}19{.}960 \dashrightarrow 00{:}36{:}21{.}850$ immune cells than what sort

NOTE Confidence: 0.830093532272727

 $00{:}36{:}21{.}913 \dashrightarrow 00{:}36{:}24{.}181$ of tolerated as myocarditis and Dallas

NOTE Confidence: 0.830093532272727

 $00:36:24.181 \rightarrow 00:36:26.500$ are meaningful to that bad outcome.

NOTE Confidence: 0.830093532272727

 $00:36:26.500 \longrightarrow 00:36:28.792$ So you don't have to necessarily

 $00{:}36{:}28.792 \dashrightarrow 00{:}36{:}30.973$ see myocarditis with injury to get

NOTE Confidence: 0.830093532272727

00:36:30.973 - > 00:36:32.731 to a biopsy where that patient

NOTE Confidence: 0.830093532272727

 $00:36:32.731 \longrightarrow 00:36:34.718$ is going to have that outcome.

NOTE Confidence: 0.830093532272727

 $00:36:34.720 \rightarrow 00:36:36.603$ I think that same data is supported

NOTE Confidence: 0.830093532272727

 $00{:}36{:}36{.}603 \dashrightarrow 00{:}36{:}39{.}049$ here from a paper out of Japan and

NOTE Confidence: 0.830093532272727

 $00:36:39.049 \rightarrow 00:36:40.624$ Cirque Journal where they looked

NOTE Confidence: 0.830093532272727

00:36:40.687 --> 00:36:43.536 at people who had what they called

NOTE Confidence: 0.830093532272727

 $00:36:43.536 \rightarrow 00:36:44.757$ inflammatory dilated cardiomyopathy,

NOTE Confidence: 0.830093532272727

 $00{:}36{:}44.760 \dashrightarrow 00{:}36{:}46.489$ meaning they saw too many immune cells

NOTE Confidence: 0.830093532272727

 $00:36:46.489 \rightarrow 00:36:48.499$ in the setting of dilated cardiomyopathy.

NOTE Confidence: 0.830093532272727

 $00:36:48.500 \rightarrow 00:36:50.817$ Which is probably very similar or the

NOTE Confidence: 0.830093532272727

 $00{:}36{:}50{.}817 \dashrightarrow 00{:}36{:}53{.}369$ same thing as borderline myocarditis.

NOTE Confidence: 0.830093532272727

 $00:36:53.370 \rightarrow 00:36:56.466$ And where they had more CD3 positive cells,

NOTE Confidence: 0.830093532272727

 $00{:}36{:}56{.}470 \dashrightarrow 00{:}36{:}58{.}490$ those patients had worse outcomes,

NOTE Confidence: 0.830093532272727

 $00{:}36{:}58{.}490 \dashrightarrow 00{:}37{:}01{.}290$ less survival free of cardiac death or

 $00:37:01.290 \rightarrow 00:37:03.889$ left ventricular cyst device implantation.

NOTE Confidence: 0.830093532272727

 $00:37:03.890 \longrightarrow 00:37:05.350$ Where they saw fewer cells,

NOTE Confidence: 0.830093532272727

00:37:05.350 - 00:37:06.694 those patients did better.

NOTE Confidence: 0.830093532272727

 $00:37:06.694 \longrightarrow 00:37:09.547$ Now note, it did take about 9 years to

NOTE Confidence: 0.830093532272727

 $00:37:09.547 \longrightarrow 00:37:12.230$ see like these really big differences.

NOTE Confidence: 0.830093532272727

 $00{:}37{:}12.230 \dashrightarrow 00{:}37{:}14.330$ That's just a pretty long prediction

NOTE Confidence: 0.830093532272727

00:37:14.330 --> 00:37:15.030 in advance,

NOTE Confidence: 0.830093532272727

 $00:37:15.030 \longrightarrow 00:37:17.144$ but it does tell us that more

NOTE Confidence: 0.830093532272727

 $00{:}37{:}17.144 \dashrightarrow 00{:}37{:}18.510$ immune cells are worse.

NOTE Confidence: 0.830093532272727

 $00{:}37{:}18{.}510 \dashrightarrow 00{:}37{:}19{.}044$ And fewer.

NOTE Confidence: 0.830093532272727

 $00:37:19.044 \dashrightarrow 00:37:20.646$ So it's something we should be

NOTE Confidence: 0.830093532272727

 $00:37:20.646 \rightarrow 00:37:22.518$ cognizant of when we make new criteria,

NOTE Confidence: 0.830093532272727

 $00:37:22.520 \longrightarrow 00:37:26.276$ not look to lump everything together.

NOTE Confidence: 0.830093532272727

 $00{:}37{:}26.280 \dashrightarrow 00{:}37{:}29.700$ So we decided to go after this and these

NOTE Confidence: 0.830093532272727

 $00:37:29.700 \rightarrow 00:37:33.537$ are the goals that we set up for ourselves,

NOTE Confidence: 0.830093532272727

 $00:37:33.540 \longrightarrow 00:37:35.628$ very similar to what the opportunities

- NOTE Confidence: 0.830093532272727
- $00:37:35.628 \rightarrow 00:37:37.804$ were to develop revised biopsy criteria
- NOTE Confidence: 0.830093532272727
- $00:37:37.804 \rightarrow 00:37:40.338$ for a better definition of myocyte injury,
- NOTE Confidence: 0.830093532272727
- 00:37:40.340 --> 00:37:42.440 better incorporation of immunohistochemistry,
- NOTE Confidence: 0.830093532272727
- $00{:}37{:}42{.}440 \dashrightarrow 00{:}37{:}45{.}590$ better classification based on the extent
- NOTE Confidence: 0.830093532272727
- $00:37:45.654 \rightarrow 00:37:47.644$ of injury and better classification
- NOTE Confidence: 0.830093532272727
- $00:37:47.644 \rightarrow 00:37:49.634$ based on types of myocarditis.
- NOTE Confidence: 0.830093532272727
- $00:37:49.640 \longrightarrow 00:37:51.644$ So that's what we're doing on
- NOTE Confidence: 0.830093532272727
- $00:37:51.644 \longrightarrow 00:37:52.646$ the biopsy side.
- NOTE Confidence: 0.830093532272727
- $00{:}37{:}52.650 \dashrightarrow 00{:}37{:}55.236$ On the autopsy or explant side,
- NOTE Confidence: 0.830093532272727
- $00:37:55.240 \longrightarrow 00:37:56.284$ it's to define.
- NOTE Confidence: 0.830093532272727
- $00:37:56.284 \rightarrow 00:37:58.372$ Carditis based on evaluation of the
- NOTE Confidence: 0.830093532272727
- $00{:}37{:}58{.}372 \dashrightarrow 00{:}38{:}00{.}731$ whole heart and to synergize this
- NOTE Confidence: 0.830093532272727
- $00:38:00.731 \rightarrow 00:38:02.681$ terminology with the biopsy criteria
- NOTE Confidence: 0.830093532272727
- 00:38:02.749 --> 00:38:05.227 and ultimately it's to validate all of
- NOTE Confidence: 0.830093532272727
- $00:38:05.227 \dashrightarrow 00:38:08.870$ these criteria with historical samples.
- NOTE Confidence: 0.830093532272727

 $00:38:08.870 \rightarrow 00:38:11.383$ And so the timeline that we've been

NOTE Confidence: 0.830093532272727

00:38:11.383 --> 00:38:13.992 working on is here in March of 2023,

NOTE Confidence: 0.830093532272727

 $00{:}38{:}13.992 \dashrightarrow 00{:}38{:}16.248$ we met at the use CAP meeting and

NOTE Confidence: 0.830093532272727

 $00{:}38{:}16{.}248 \dashrightarrow 00{:}38{:}18{.}524$ developed consensus that we wanted to go

NOTE Confidence: 0.830093532272727

 $00{:}38{:}18{.}524 \dashrightarrow 00{:}38{:}20{.}800$ forward with revising the Dallas criteria.

NOTE Confidence: 0.830093532272727

 $00:38:20.800 \dashrightarrow 00:38:23.313$ The SVP and the European Society both NOTE Confidence: 0.830093532272727

 $00{:}38{:}23{.}313 \dashrightarrow 00{:}38{:}26{.}399$ agreed that we should go forward with this.

NOTE Confidence: 0.830093532272727

 $00{:}38{:}26{.}400 \dashrightarrow 00{:}38{:}29{.}438$ We then created 210 person teams to

NOTE Confidence: 0.830093532272727

 $00:38:29.438 \rightarrow 00:38:32.349$ work on generating these new criteria.

NOTE Confidence: 0.830093532272727

 $00:38:32.350 \dashrightarrow 00:38:33.850$ It started with the literature review.

NOTE Confidence: 0.830093532272727

 $00{:}38{:}33{.}850 \dashrightarrow 00{:}38{:}35{.}250$ I showed you a couple of examples,

NOTE Confidence: 0.830093532272727

00:38:35.250 --> 00:38:37.590 but we grabbed hunt, not hundreds,

NOTE Confidence: 0.830093532272727

 $00{:}38{:}37{.}590 \dashrightarrow 00{:}38{:}38{.}850$ that's too many, but.

NOTE Confidence: 0.830093532272727

 $00:38:38.850 \longrightarrow 00:38:40.740$ Scores and scores of papers that

NOTE Confidence: 0.830093532272727

 $00:38:40.801 \longrightarrow 00:38:41.560$ we then read,

NOTE Confidence: 0.830093532272727

 $00:38:41.560 \dashrightarrow 00:38:44.130$ evaluated and sort of discussed

 $00:38:44.130 \longrightarrow 00:38:45.158$ amongst ourselves.

NOTE Confidence: 0.830093532272727

 $00{:}38{:}45{.}160 \dashrightarrow 00{:}38{:}46{.}894$ We then did an adelphic question

NOTE Confidence: 0.830093532272727

 $00{:}38{:}46{.}894 \dashrightarrow 00{:}38{:}49{.}075$ and answer where we took like the

NOTE Confidence: 0.830093532272727

00:38:49.075 - 00:38:50.675 key questions related to biopsy,

NOTE Confidence: 0.830093532272727

 $00:38:50.680 \rightarrow 00:38:52.768$ sent them out to everybody in the group

NOTE Confidence: 0.830093532272727

 $00:38:52.768 \rightarrow 00:38:55.019$ and got everyone's anonymous feedback.

NOTE Confidence: 0.830093532272727

 $00:38:55.020 \dashrightarrow 00:38:58.524$ And then saw what sort of where people

NOTE Confidence: 0.830093532272727

 $00:38:58.524 \dashrightarrow 00:39:01.209$ were based on their own beliefs

NOTE Confidence: 0.830093532272727

 $00:39:01.209 \dashrightarrow 00:39:03.375$ and experiences and ask people to

NOTE Confidence: 0.830093532272727

 $00:39:03.375 \longrightarrow 00:39:05.350$ find the data that supported it.

NOTE Confidence: 0.830093532272727

00:39:05.350 --> 00:39:07.036 Because if this is not data-driven,

NOTE Confidence: 0.830093532272727

 $00{:}39{:}07{.}040 \dashrightarrow 00{:}39{:}10{.}024$ it's probably not worth doing in my opinion.

NOTE Confidence: 0.830093532272727

 $00:39:10.030 \rightarrow 00:39:12.536$ Our goal is to have preliminary criteria

NOTE Confidence: 0.830093532272727

 $00{:}39{:}12{.}536 \dashrightarrow 00{:}39{:}15{.}100$ for both of these by March of 2023.

NOTE Confidence: 0.830093532272727

00:39:15.100 - 00:39:16.350 And on the biopsy side,

 $00:39:16.350 \longrightarrow 00:39:18.276$ we've already split into three or

NOTE Confidence: 0.830093532272727

00:39:18.276 --> 00:39:20.164 four groups to work on criteria

NOTE Confidence: 0.830093532272727

 $00:39:20.164 \rightarrow 00:39:22.234$ ideas independently which we're going

NOTE Confidence: 0.830093532272727

 $00:39:22.234 \rightarrow 00:39:24.760$ to bring together and have by the

NOTE Confidence: 0.830093532272727

 $00{:}39{:}24.760 \dashrightarrow 00{:}39{:}26.636$ use CAP meeting and then spend a

NOTE Confidence: 0.81884808826087

 $00:39:26.700 \longrightarrow 00:39:27.978$ year evaluating this.

NOTE Confidence: 0.81884808826087

 $00{:}39{:}27{.}980 \dashrightarrow 00{:}39{:}30{.}140$ We want to kick the tires on these criteria.

NOTE Confidence: 0.81884808826087

 $00:39:30.140 \rightarrow 00:39:32.748$ We're going to go back to historical data,

NOTE Confidence: 0.81884808826087

00:39:32.750 --> 00:39:33.798 Johns Hopkins Place where

NOTE Confidence: 0.81884808826087

 $00:39:33.798 \longrightarrow 00:39:35.108$ we have historically done a

NOTE Confidence: 0.81884808826087

 $00{:}39{:}35{.}108 \dashrightarrow 00{:}39{:}36{.}528$ lot of MRI cardiac biopsies.

NOTE Confidence: 0.81884808826087

 $00{:}39{:}36{.}530 \dashrightarrow 00{:}39{:}38{.}714$ I mentioned Karen Klingle and Germany

NOTE Confidence: 0.81884808826087

 $00:39:38.714 \rightarrow 00:39:41.560$ having so many cases you wouldn't believe.

NOTE Confidence: 0.81884808826087

 $00:39:41.560 \rightarrow 00:39:44.185$ And seeing if the criteria that we've

NOTE Confidence: 0.81884808826087

 $00:39:44.185 \longrightarrow 00:39:46.602$ generated with have meaningful outcome or

NOTE Confidence: 0.81884808826087

 $00:39:46.602 \rightarrow 00:39:49.458$ usefulness relative to where we are now.

- NOTE Confidence: 0.81884808826087
- $00{:}39{:}49{.}460 \dashrightarrow 00{:}39{:}51{.}556$ And some of the things that we've been

 $00{:}39{:}51{.}556$ --> $00{:}39{:}53{.}517$ playing with are in the Dallas criteria,

NOTE Confidence: 0.81884808826087

 $00:39:53.520 \rightarrow 00:39:55.092$ expanding that borderline myocarditis

NOTE Confidence: 0.81884808826087

 $00:39:55.092 \rightarrow 00:39:58.279$ to maybe a low and a high number

NOTE Confidence: 0.81884808826087

 $00:39:58.279 \rightarrow 00:39:59.416$ of immune cells,

NOTE Confidence: 0.81884808826087

 $00{:}39{:}59{.}420 \dashrightarrow 00{:}40{:}01{.}412$ better defining whether these are diffuse

NOTE Confidence: 0.81884808826087

 $00{:}40{:}01{.}412 \dashrightarrow 00{:}40{:}03{.}598$ immune cells or clusters of immune cells.

NOTE Confidence: 0.81884808826087

 $00{:}40{:}03.600 \dashrightarrow 00{:}40{:}05.427$ But these are all things we need

NOTE Confidence: 0.81884808826087

 $00:40:05.427 \longrightarrow 00:40:06.961$ to really evaluate and see how

NOTE Confidence: 0.81884808826087

 $00:40:06.961 \rightarrow 00:40:08.359$ they're going to work for us.

NOTE Confidence: 0.81884808826087

00:40:08.360 --> 00:40:10.004 And then in March of 2024,

NOTE Confidence: 0.81884808826087

 $00:40:10.004 \rightarrow 00:40:11.708$ again in conjunction with the use.

NOTE Confidence: 0.81884808826087

 $00:40:11.710 \longrightarrow 00:40:12.815$ That meeting which is going

NOTE Confidence: 0.81884808826087

 $00{:}40{:}12.815 \dashrightarrow 00{:}40{:}13.699$ to be in Baltimore,

NOTE Confidence: 0.81884808826087

 $00:40:13.700 \longrightarrow 00:40:16.157$ we're gonna have a one day event
$00:40:16.157 \rightarrow 00:40:17.983$ to hopefully introduce the criteria

NOTE Confidence: 0.81884808826087

 $00{:}40{:}17.983 \dashrightarrow 00{:}40{:}20.440$ to the larger world and take last

NOTE Confidence: 0.81884808826087

 $00:40:20.440 \longrightarrow 00:40:22.457$ feedback on them from a wider

NOTE Confidence: 0.81884808826087

 $00:40:22.457 \rightarrow 00:40:24.368$ audience as whether these are useful.

NOTE Confidence: 0.81884808826087

 $00:40:24.368 \longrightarrow 00:40:26.216$ So all this is to say,

NOTE Confidence: 0.81884808826087

00:40:26.220 --> 00:40:27.810 we've been using the Dallas criteria

NOTE Confidence: 0.81884808826087

 $00:40:27.810 \longrightarrow 00:40:30.143$ for far too long and we are finally

NOTE Confidence: 0.81884808826087

 $00:40:30.143 \longrightarrow 00:40:31.668$ getting around to optimizing and

NOTE Confidence: 0.81884808826087

 $00{:}40{:}31.668 \dashrightarrow 00{:}40{:}33.143$ improving them and we're very

NOTE Confidence: 0.81884808826087

 $00:40:33.143 \longrightarrow 00:40:33.980$ excited about this,

NOTE Confidence: 0.81884808826087

 $00:40:33.980 \longrightarrow 00:40:37.228$ what we hope is a good change

NOTE Confidence: 0.81884808826087

00:40:37.228 --> 00:40:39.720 for myocarditis. Now.

NOTE Confidence: 0.81884808826087

 $00:40:39.720 \longrightarrow 00:40:42.180$ That's one thing that we're doing.

NOTE Confidence: 0.81884808826087

 $00{:}40{:}42.180 \dashrightarrow 00{:}40{:}44.852$ The next last thing I want to talk

NOTE Confidence: 0.81884808826087

 $00:40:44.852 \rightarrow 00:40:46.935$ about is diagnosing myocarditis

NOTE Confidence: 0.81884808826087

 $00:40:46.935 \rightarrow 00:40:48.939$ beyond immune cells.

- NOTE Confidence: 0.81884808826087
- 00:40:48.940 --> 00:40:50.626 And what I really haven't mentioned
- NOTE Confidence: 0.81884808826087
- $00{:}40{:}50.626 \dashrightarrow 00{:}40{:}52.691$ so far is that myocarditis is
- NOTE Confidence: 0.81884808826087
- $00:40:52.691 \longrightarrow 00:40:54.008$ a heterogeneous disease.
- NOTE Confidence: 0.81884808826087
- $00{:}40{:}54.010 \dashrightarrow 00{:}40{:}56.206$ And so when sometimes when that
- NOTE Confidence: 0.81884808826087
- 00:40:56.206 --> 00:40:57.304 endomyocardial biopsy plucks
- NOTE Confidence: 0.81884808826087
- $00{:}40{:}57{.}304 \dashrightarrow 00{:}40{:}59{.}111$ those little bits of tissue from
- NOTE Confidence: 0.81884808826087
- 00:40:59.111 00:41:00.496 the side of the septum,
- NOTE Confidence: 0.81884808826087
- $00:41:00.500 \longrightarrow 00:41:03.180$ it might miss that infiltrate.
- NOTE Confidence: 0.81884808826087
- $00{:}41{:}03{.}180 \dashrightarrow 00{:}41{:}05{.}378$ So The Dirty little secret in biopsying
- NOTE Confidence: 0.81884808826087
- $00:41:05.378 \rightarrow 00:41:07.848$ is we're only good at finding myocarditis
- NOTE Confidence: 0.81884808826087
- $00:41:07.848 \longrightarrow 00:41:09.780$ about 50% of the time when it's there.
- NOTE Confidence: 0.81884808826087
- 00:41:09.780 --> 00:41:12.210 And this is based on a study where they
- NOTE Confidence: 0.81884808826087
- $00{:}41{:}12{.}210 \dashrightarrow 00{:}41{:}14{.}757$ took autopsy hearts that had myocarditis,
- NOTE Confidence: 0.81884808826087
- $00{:}41{:}14{.}760 \dashrightarrow 00{:}41{:}16.832$ took a case bioptome and pulled little
- NOTE Confidence: 0.81884808826087
- $00{:}41{:}16.832 \dashrightarrow 00{:}41{:}19.456$ pieces off the septum and saw how frequently.
- NOTE Confidence: 0.81884808826087

 $00:41:19.460 \longrightarrow 00:41:21.434$ They can make the diagnosis and

NOTE Confidence: 0.81884808826087

 $00:41:21.434 \rightarrow 00:41:23.459$ actually the more pieces the better.

NOTE Confidence: 0.81884808826087

 $00:41:23.460 \longrightarrow 00:41:25.080$ 5 being better than three.

NOTE Confidence: 0.81884808826087

00:41:25.080 --> 00:41:25.626 My institution,

NOTE Confidence: 0.81884808826087

 $00:41:25.626 \longrightarrow 00:41:26.718$ they give me 3.

NOTE Confidence: 0.81884808826087

 $00:41:26.720 \longrightarrow 00:41:29.106$ So maybe we're only 30% good at

NOTE Confidence: 0.81884808826087

 $00:41:29.106 \longrightarrow 00:41:29.752$ finding myocarditis.

NOTE Confidence: 0.81884808826087

 $00{:}41{:}29.752 \dashrightarrow 00{:}41{:}32.637$ So it is a problem because we can miss it.

NOTE Confidence: 0.81884808826087

 $00{:}41{:}32.640 \dashrightarrow 00{:}41{:}35.232$ We could be just next to it and miss

NOTE Confidence: 0.81884808826087

 $00{:}41{:}35{.}232 \dashrightarrow 00{:}41{:}38{.}041$ it or what we're calling borderline

NOTE Confidence: 0.81884808826087

 $00:41:38.041 \rightarrow 00:41:41.300$ myocarditis could be really close to injury,

NOTE Confidence: 0.81884808826087

 $00:41:41.300 \rightarrow 00:41:43.076$ but always here a few cells,

NOTE Confidence: 0.81884808826087

 $00{:}41{:}43.080 \dashrightarrow 00{:}41{:}44.400$ but also for borderline.

NOTE Confidence: 0.81884808826087

 $00{:}41{:}44{.}400 \dashrightarrow 00{:}41{:}46{.}380$ And I didn't say this before,

NOTE Confidence: 0.81884808826087

00:41:46.380 --> 00:41:48.532 anybody of my age or older is going

NOTE Confidence: 0.81884808826087

 $00:41:48.532 \rightarrow 00:41:50.898$ to have a collection of lymphocytes.

- NOTE Confidence: 0.81884808826087
- $00:41:50.900 \longrightarrow 00:41:51.900$ Somewhere in their heart.
- NOTE Confidence: 0.81884808826087
- $00:41:51.900 \longrightarrow 00:41:53.400$ If you take enough samples of
- NOTE Confidence: 0.81884808826087
- $00:41:53.455 \rightarrow 00:41:54.547$ someone's heart over 50,
- NOTE Confidence: 0.81884808826087
- $00:41:54.550 \rightarrow 00:41:55.768$ you're going to see a collection.
- NOTE Confidence: 0.81884808826087
- $00:41:55.770 \longrightarrow 00:41:56.862$ Is that meaningful?
- NOTE Confidence: 0.81884808826087
- $00:41:56.862 \longrightarrow 00:41:57.590$ Probably not.
- NOTE Confidence: 0.81884808826087
- $00{:}41{:}57{.}590 \dashrightarrow 00{:}41{:}59{.}802$ So it's either a random collection that
- NOTE Confidence: 0.81884808826087
- $00:41:59.802 \rightarrow 00:42:02.128$ you bump into by accident on biopsy,
- NOTE Confidence: 0.81884808826087
- $00:42:02.130 \longrightarrow 00:42:04.866$ or is the tip of the iceberg and
- NOTE Confidence: 0.81884808826087
- $00:42:04.866 \rightarrow 00:42:07.578$ you're just missing something nearby.
- NOTE Confidence: 0.81884808826087
- $00:42:07.580 \longrightarrow 00:42:10.380$ So what we've started to think about is,
- NOTE Confidence: 0.81884808826087
- $00{:}42{:}10{.}380 \dashrightarrow 00{:}42{:}12{.}172$ let's say this is a biopsy that
- NOTE Confidence: 0.81884808826087
- $00:42:12.172 \longrightarrow 00:42:12.940$ was performed this
- NOTE Confidence: 0.878341105833333
- $00{:}42{:}12{.}996 \dashrightarrow 00{:}42{:}15{.}860$ number one, and that star represents an
- NOTE Confidence: 0.878341105833333
- $00:42:15.860 \rightarrow 00:42:18.780$ area of inflammation and myocyte injury.
- NOTE Confidence: 0.878341105833333

00:42:18.780 --> 00:42:20.778 If you biopsy that by Histology,

NOTE Confidence: 0.878341105833333

00:42:20.780 --> 00:42:22.100 you're going to be able

NOTE Confidence: 0.878341105833333

 $00:42:22.100 \longrightarrow 00:42:23.156$ to make the diagnosis.

NOTE Confidence: 0.878341105833333

 $00:42:23.160 \rightarrow 00:42:25.435$ But we also suspect that the cells,

NOTE Confidence: 0.878341105833333

 $00{:}42{:}25{.}440 \dashrightarrow 00{:}42{:}27{.}414$ the native cells in the heart

NOTE Confidence: 0.878341105833333

 $00{:}42{:}27{.}414 \dashrightarrow 00{:}42{:}29{.}197$ are probably responding to that

NOTE Confidence: 0.878341105833333

00:42:29.197 --> 00:42:30.797 immune infiltrate and injury.

NOTE Confidence: 0.878341105833333

 $00:42:30.800 \longrightarrow 00:42:32.468$ The myocytes themselves,

NOTE Confidence: 0.878341105833333

 $00:42:32.468 \longrightarrow 00:42:34.136$ the endothelial cells,

NOTE Confidence: 0.878341105833333

 $00:42:34.140 \longrightarrow 00:42:35.202$ the native fibroblasts,

NOTE Confidence: 0.878341105833333

 $00{:}42{:}35{.}202 \dashrightarrow 00{:}42{:}38{.}165$ they may be sensing this damage in this

NOTE Confidence: 0.878341105833333

 $00:42:38.165 \rightarrow 00:42:40.679$ process and changing their signaling state.

NOTE Confidence: 0.878341105833333

 $00:42:40.680 \longrightarrow 00:42:42.878$ And the question is can we identify

NOTE Confidence: 0.878341105833333

 $00{:}42{:}42{.}878 \dashrightarrow 00{:}42{:}45{.}250$ what that is and can we capture

NOTE Confidence: 0.878341105833333

 $00{:}42{:}45{.}250 \dashrightarrow 00{:}42{:}47{.}290$ that information so if we instead

NOTE Confidence: 0.878341105833333

 $00:42:47.363 \rightarrow 00:42:49.589$ of biopsying this piece of tissue?

- NOTE Confidence: 0.878341105833333
- 00:42:49.590 --> 00:42:51.720 I'm biopsying this piece of tissue,
- NOTE Confidence: 0.878341105833333
- $00:42:51.720 \longrightarrow 00:42:53.460$ but whatever this process is,
- NOTE Confidence: 0.878341105833333
- $00:42:53.460 \longrightarrow 00:42:55.110$ is sending out a signal
- NOTE Confidence: 0.878341105833333
- $00:42:55.110 \longrightarrow 00:42:56.760$ really wide out to here.
- NOTE Confidence: 0.878341105833333
- $00{:}42{:}56.760 \dashrightarrow 00{:}42{:}59.560$ Maybe I can still sense that signal
- NOTE Confidence: 0.878341105833333
- $00:42:59.560 \rightarrow 00:43:01.779$ adjacent that's going to increase
- NOTE Confidence: 0.878341105833333
- $00{:}43{:}01.779 \dashrightarrow 00{:}43{:}04.134$ our yield on endomyocardial biopsy.
- NOTE Confidence: 0.878341105833333
- $00{:}43{:}04{.}140 \dashrightarrow 00{:}43{:}06{.}219$ Now this won't be necessary for cases
- NOTE Confidence: 0.878341105833333
- $00:43:06.219 \rightarrow 00:43:08.141$ where very obvious myocarditis could be
- NOTE Confidence: 0.878341105833333
- $00:43:08.141 \rightarrow 00:43:10.409$ rendered even if my experts don't agree,
- NOTE Confidence: 0.878341105833333
- $00:43:10.410 \longrightarrow 00:43:11.586$ but can get close.
- NOTE Confidence: 0.878341105833333
- 00:43:11.586 --> 00:43:13.350 It will be useful in scenarios
- NOTE Confidence: 0.878341105833333
- $00{:}43{:}13.416 \dashrightarrow 00{:}43{:}15.360$ where there is a borderline type
- NOTE Confidence: 0.878341105833333
- 00:43:15.360 --> 00:43:17.371 of diagnosis where we see some
- NOTE Confidence: 0.878341105833333
- $00{:}43{:}17{.}371 \dashrightarrow 00{:}43{:}19{.}315$ inflammation but don't see enough to
- NOTE Confidence: 0.878341105833333

 $00:43:19.315 \rightarrow 00:43:21.089$ make the diagnosis of myocarditis.

NOTE Confidence: 0.878341105833333

00:43:21.089 --> 00:43:23.327 Or in certain clinical scenarios where

NOTE Confidence: 0.878341105833333

 $00:43:23.327 \rightarrow 00:43:25.570$ the suspicion is very high and again,

NOTE Confidence: 0.878341105833333

 $00:43:25.570 \rightarrow 00:43:29.259$ we might have just missed that material.

NOTE Confidence: 0.878341105833333

 $00:43:29.260 \longrightarrow 00:43:31.752$ Now this has probably been a long

NOTE Confidence: 0.878341105833333

 $00{:}43{:}31{.}752 \dashrightarrow 00{:}43{:}34{.}420$ standing dream for a for years and

NOTE Confidence: 0.878341105833333

 $00:43:34.420 \longrightarrow 00:43:36.335$ it's known that cardiac myocytes

NOTE Confidence: 0.878341105833333

 $00:43:36.335 \rightarrow 00:43:38.570$ respond to inflammation and induce

NOTE Confidence: 0.878341105833333

 $00:43:38.570 \rightarrow 00:43:41.240$ their own cytokines to cardiac injury.

NOTE Confidence: 0.878341105833333

 $00:43:41.240 \longrightarrow 00:43:42.983$ As you can see in this nice

NOTE Confidence: 0.878341105833333

 $00:43:42.983 \longrightarrow 00:43:44.359$ review from some years ago.

NOTE Confidence: 0.878341105833333

 $00{:}43{:}44{.}360 \dashrightarrow 00{:}43{:}47{.}372$ And this is a paper from 2004 showing

NOTE Confidence: 0.878341105833333

 $00{:}43{:}47{.}372 \dashrightarrow 00{:}43{:}50{.}424$ that tissue necrosis factor alpha or TNF

NOTE Confidence: 0.878341105833333

 $00:43:50.424 \rightarrow 00:43:53.379$ alpha is increased in cardiac myocytes.

NOTE Confidence: 0.878341105833333

 $00:43:53.380 \longrightarrow 00:43:55.214$ So you can see that here and

NOTE Confidence: 0.878341105833333

 $00:43:55.214 \rightarrow 00:43:57.414$ that's sort of a sign that these

- NOTE Confidence: 0.878341105833333
- $00:43:57.414 \rightarrow 00:43:59.104$ cells are changing their immune.
- NOTE Confidence: 0.878341105833333
- $00:43:59.110 \longrightarrow 00:43:59.547$ Response.
- NOTE Confidence: 0.878341105833333
- 00:43:59.547 --> 00:44:00.421 However, historically,
- NOTE Confidence: 0.878341105833333
- $00:44:00.421 \rightarrow 00:44:03.480$ if we wanted to look for differences
- NOTE Confidence: 0.878341105833333
- $00:44:03.550 \rightarrow 00:44:05.770$ between disease and normal tissues,
- NOTE Confidence: 0.878341105833333
- $00:44:05.770 \longrightarrow 00:44:06.822$ we get the tissues,
- NOTE Confidence: 0.878341105833333
- $00:44:06.822 \rightarrow 00:44:07.874$ we grind it up,
- NOTE Confidence: 0.878341105833333
- $00:44:07.880 \rightarrow 00:44:09.866$ we look for gene expression differences,
- NOTE Confidence: 0.878341105833333
- $00:44:09.870 \longrightarrow 00:44:10.544$ very straightforward.
- NOTE Confidence: 0.878341105833333
- $00:44:10.544 \longrightarrow 00:44:13.240$ But if you have a lot of immune
- NOTE Confidence: 0.878341105833333
- 00:44:13.309 --> 00:44:14.710 cells infiltrating in,
- NOTE Confidence: 0.878341105833333
- 00:44:14.710 --> 00:44:16.408 that big immune signal you're going
- NOTE Confidence: 0.878341105833333
- $00:44:16.408 \rightarrow 00:44:18.526$ to see is really mostly coming from
- NOTE Confidence: 0.878341105833333
- $00{:}44{:}18.526 \dashrightarrow 00{:}44{:}20.696$ those immune cells and you're going to
- NOTE Confidence: 0.878341105833333
- $00{:}44{:}20.754 \dashrightarrow 00{:}44{:}22.776$ be missing the more subtle potentially
- NOTE Confidence: 0.878341105833333

 $00:44:22.776 \rightarrow 00:44:25.550$ signals that are coming from myocytes,

NOTE Confidence: 0.878341105833333

00:44:25.550 --> 00:44:26.260 fibroblasts,

NOTE Confidence: 0.878341105833333

 $00:44:26.260 \longrightarrow 00:44:28.390$ endothelial cells relative.

NOTE Confidence: 0.878341105833333

 $00:44:28.390 \rightarrow 00:44:30.466$ So that's always been a challenge

NOTE Confidence: 0.878341105833333

 $00{:}44{:}30{.}466 \dashrightarrow 00{:}44{:}31{.}850$ we can't really assign.

NOTE Confidence: 0.878341105833333

 $00:44:31.850 \longrightarrow 00:44:33.670$ Those signals to this the

NOTE Confidence: 0.878341105833333

 $00:44:33.670 \longrightarrow 00:44:35.800$ cells we want to look at.

NOTE Confidence: 0.878341105833333

 $00{:}44{:}35{.}800 \dashrightarrow 00{:}44{:}37{.}720$ So that's where spatial transcriptomics

NOTE Confidence: 0.878341105833333

 $00:44:37.720 \longrightarrow 00:44:39.640$ can potentially help us out.

NOTE Confidence: 0.878341105833333

 $00:44:39.640 \longrightarrow 00:44:39.956$ OK.

NOTE Confidence: 0.878341105833333

 $00{:}44{:}39{.}956 \dashrightarrow 00{:}44{:}42{.}168$ So we have started to do some

NOTE Confidence: 0.878341105833333

 $00:44:42.168 \longrightarrow 00:44:43.977$ work in collaboration with

NOTE Confidence: 0.878341105833333

00:44:43.977 --> 00:44:46.727 Luigi Adamo and Kevin Partilla.

NOTE Confidence: 0.878341105833333

00:44:46.730 --> 00:44:48.746 And we're using a method called

NOTE Confidence: 0.878341105833333

 $00:44:48.750 \rightarrow 00:44:51.414$ 10X Vizio and what it does is you

NOTE Confidence: 0.878341105833333

 $00:44:51.414 \rightarrow 00:44:54.117$ can see in this top left corner.

- NOTE Confidence: 0.878341105833333
- $00:44:54.120 \longrightarrow 00:44:55.840$ This is a glass slide and you can
- NOTE Confidence: 0.878341105833333
- $00:44:55.840 \longrightarrow 00:44:57.976$ put 4 slices of tissue on the slide,
- NOTE Confidence: 0.878341105833333
- $00:44:57.980 \longrightarrow 00:44:59.450$ which is shown actually here.
- NOTE Confidence: 0.878341105833333
- $00:44:59.450 \rightarrow 00:45:01.922$ These are endomyocardial biopsies.
- NOTE Confidence: 0.878341105833333
- $00:45:01.922 \longrightarrow 00:45:04.394$ And across those squares,
- NOTE Confidence: 0.878341105833333
- $00:45:04.400 \longrightarrow 00:45:06.480$ there's like a barcode address
- NOTE Confidence: 0.878341105833333
- $00:45:06.480 \longrightarrow 00:45:09.339$ for each 55 Micron core or space.
- NOTE Confidence: 0.878341105833333
- $00:45:09.340 \longrightarrow 00:45:10.666$ And then the tissue that's put
- NOTE Confidence: 0.878341105833333
- 00:45:10.666 --> 00:45:11.860 up on top of that,
- NOTE Confidence: 0.878341105833333
- 00:45:11.860 --> 00:45:14.866 we identify what the RNAs are.
- NOTE Confidence: 0.878341105833333
- 00:45:14.870 --> 00:45:15.207 They're,
- NOTE Confidence: 0.878341105833333
- $00:45:15.207 \longrightarrow 00:45:16.555$ they're tagged with that
- NOTE Confidence: 0.878341105833333
- $00{:}45{:}16.555 \dashrightarrow 00{:}45{:}18.240$ barcode of where that's located
- NOTE Confidence: 0.696277422142857
- $00{:}45{:}18.298 \dashrightarrow 00{:}45{:}19.698$ and then they're sequenced.
- NOTE Confidence: 0.696277422142857
- $00{:}45{:}19.700 \dashrightarrow 00{:}45{:}21.548$ And so we know what the expression
- NOTE Confidence: 0.696277422142857

 $00:45:21.548 \longrightarrow 00:45:23.573$ is in each one of those regions

NOTE Confidence: 0.696277422142857

 $00{:}45{:}23.573 \dashrightarrow 00{:}45{:}25.518$ all the way across. The tissue.

NOTE Confidence: 0.696277422142857

 $00{:}45{:}25{.}518 \dashrightarrow 00{:}45{:}27{.}416$ And so that's this particular

NOTE Confidence: 0.696277422142857

 $00:45:27.416 \rightarrow 00:45:28.908$ type of spatial transcriptomics

NOTE Confidence: 0.696277422142857

 $00:45:28.908 \longrightarrow 00:45:30.730$ or other approaches as well.

NOTE Confidence: 0.696277422142857

 $00{:}45{:}30{.}730 \dashrightarrow 00{:}45{:}33{.}090$ And I'm gonna stop for a second and

NOTE Confidence: 0.696277422142857

 $00:45:33.090 \rightarrow 00:45:35.787$ get on my soapbox and say something.

NOTE Confidence: 0.696277422142857

 $00:45:35.790 \longrightarrow 00:45:37.330$ We as pathologists have got

NOTE Confidence: 0.696277422142857

 $00{:}45{:}37{.}330 \dashrightarrow 00{:}45{:}39{.}472$ to get engaged in this concept

NOTE Confidence: 0.696277422142857

 $00:45:39.472 \rightarrow 00:45:41.089$ of spatial transcriptomics.

NOTE Confidence: 0.696277422142857

00:45:41.090 --> 00:45:42.903 I am a member of the Human

NOTE Confidence: 0.696277422142857

 $00:45:42.903 \rightarrow 00:45:44.250$ Cell Atlas and Hub map,

NOTE Confidence: 0.696277422142857

 $00{:}45{:}44.250 \dashrightarrow 00{:}45{:}46.538$ which are two big NIH and other studies

NOTE Confidence: 0.696277422142857

 $00:45:46.538 \longrightarrow 00:45:48.274$ to identify where every cell is

NOTE Confidence: 0.696277422142857

 $00:45:48.274 \longrightarrow 00:45:50.278$ located in the human body and discover

NOTE Confidence: 0.696277422142857

 $00:45:50.278 \rightarrow 00:45:52.322$ all the cell types and there are

- NOTE Confidence: 0.696277422142857
- $00:45:52.322 \rightarrow 00:45:54.954$ not enough pathologists in the room.
- NOTE Confidence: 0.696277422142857
- $00:45:54.954 \rightarrow 00:45:56.998$ These are brilliant bioinformaticians.
- NOTE Confidence: 0.696277422142857
- $00:45:57.000 \rightarrow 00:45:58.272$ They do great science.
- NOTE Confidence: 0.696277422142857
- $00{:}45{:}58{.}272 \dashrightarrow 00{:}46{:}01{.}854$ But a lot of them don't know 110th of what
- NOTE Confidence: 0.696277422142857
- $00{:}46{:}01{.}854 \dashrightarrow 00{:}46{:}04{.}260$ you guys intuitively know about tissue.
- NOTE Confidence: 0.696277422142857
- $00{:}46{:}04{.}260 \dashrightarrow 00{:}46{:}06{.}790$ And it would be nefit all of them if we as
- NOTE Confidence: 0.696277422142857
- 00:46:06.853 --> 00:46:09.197 a society or a group get more engaged,
- NOTE Confidence: 0.696277422142857
- $00:46:09.200 \rightarrow 00:46:10.870$ particularly now that they're starting
- NOTE Confidence: 0.696277422142857
- $00{:}46{:}10.870 \dashrightarrow 00{:}46{:}12.540$ to move to spatial transcriptomics
- NOTE Confidence: 0.696277422142857
- $00:46:12.594 \longrightarrow 00:46:13.739$ and really need our help.
- NOTE Confidence: 0.696277422142857
- $00:46:13.740 \longrightarrow 00:46:15.756$ Kevin, get off my soapbox now.
- NOTE Confidence: 0.696277422142857
- 00:46:15.760 --> 00:46:17.552 But I had to say that I feel
- NOTE Confidence: 0.696277422142857
- $00:46:17.552 \longrightarrow 00:46:18.620$ very passionate about that.
- NOTE Confidence: 0.696277422142857
- $00{:}46{:}18.620 \dashrightarrow 00{:}46{:}20.083$ I sometimes go to these meetings and
- NOTE Confidence: 0.696277422142857
- $00:46:20.083 \rightarrow 00:46:21.779$ I'm the only pathologist in the room,
- NOTE Confidence: 0.696277422142857

 $00:46:21.780 \longrightarrow 00:46:24.160$ and I I often shake my head.

NOTE Confidence: 0.696277422142857

00:46:24.160 --> 00:46:25.420 OK, so but. Back to this.

NOTE Confidence: 0.696277422142857

 $00:46:25.420 \longrightarrow 00:46:27.814$ So we decided to use this approach

NOTE Confidence: 0.696277422142857

 $00:46:27.814 \longrightarrow 00:46:29.380$ now spatial this method,

NOTE Confidence: 0.696277422142857

 $00:46:29.380 \longrightarrow 00:46:32.680$ these core sizes are 55 microns,

NOTE Confidence: 0.696277422142857

 $00:46:32.680 \longrightarrow 00:46:34.184$ which is not the size of a cell.

NOTE Confidence: 0.696277422142857

 $00:46:34.190 \rightarrow 00:46:36.899$ They're bigger than a normal small cell,

NOTE Confidence: 0.696277422142857

 $00:46:36.900 \rightarrow 00:46:39.420$ but a cardiac myocyte is a big cell.

NOTE Confidence: 0.696277422142857

 $00:46:39.420 \longrightarrow 00:46:42.140$ So the match is pretty close to 1:00 to 1:00.

NOTE Confidence: 0.696277422142857

 $00:46:42.140 \longrightarrow 00:46:45.020$ So we feel good about that.

NOTE Confidence: 0.696277422142857

 $00:46:45.020 \longrightarrow 00:46:46.020$ You can see here though,

NOTE Confidence: 0.696277422142857

 $00{:}46{:}46{.}020 \dashrightarrow 00{:}46{:}47{.}376$ these are endomy ocardial biopsies

NOTE Confidence: 0.696277422142857

 $00{:}46{:}47.376 \dashrightarrow 00{:}46{:}49.071$ after we've already used them

NOTE Confidence: 0.696277422142857

 $00:46:49.071 \longrightarrow 00:46:50.379$ for clinical purposes.

NOTE Confidence: 0.696277422142857

 $00:46:50.380 \rightarrow 00:46:52.460$ So the amount of tissue left wasn't great,

NOTE Confidence: 0.696277422142857

 $00:46:52.460 \longrightarrow 00:46:54.960$ but for these are myocarditis.

- NOTE Confidence: 0.696277422142857
- $00:46:54.960 \longrightarrow 00:46:57.770$ For these are non myocarditis.
- NOTE Confidence: 0.696277422142857
- $00{:}46{:}57{.}770 \dashrightarrow 00{:}46{:}59{.}786$ We we did this with a core facility
- NOTE Confidence: 0.696277422142857
- $00{:}46{:}59{.}786 \dashrightarrow 00{:}47{:}01{.}302$ at Hopkins. We generated some data.
- NOTE Confidence: 0.696277422142857
- $00:47:01.302 \longrightarrow 00:47:03.069$ The first thing I always like to
- NOTE Confidence: 0.696277422142857
- $00{:}47{:}03.069 \dashrightarrow 00{:}47{:}04.483$ do with data is kick the tires,
- NOTE Confidence: 0.696277422142857
- $00{:}47{:}04{.}490 \dashrightarrow 00{:}47{:}06{.}254$ make sure that it seems reasonable and
- NOTE Confidence: 0.696277422142857
- 00:47:06.254 --> 00:47:08.570 it actually did. I was pretty happy.
- NOTE Confidence: 0.696277422142857
- $00:47:08.570 \rightarrow 00:47:10.520$ These are two macrophage markers,
- NOTE Confidence: 0.833239409166667
- $00{:}47{:}12.950 \dashrightarrow 00{:}47{:}14.360$ CD74TSB4X and you can see
- NOTE Confidence: 0.833239409166667
- $00:47:14.360 \longrightarrow 00:47:16.250$ where one was high in a core,
- NOTE Confidence: 0.833239409166667
- $00:47:16.250 \longrightarrow 00:47:17.307$ the other was high in a core.
- NOTE Confidence: 0.833239409166667
- $00{:}47{:}17{.}310 \dashrightarrow 00{:}47{:}19{.}170$ Each one of these dots represents
- NOTE Confidence: 0.833239409166667
- $00{:}47{:}19.170 \dashrightarrow 00{:}47{:}21.310$ a core from across these tissues.
- NOTE Confidence: 0.833239409166667
- 00:47:21.310 --> 00:47:23.575 These are two markers of
- NOTE Confidence: 0.833239409166667
- 00:47:23.575 -> 00:47:25.387 cardiac myocytes tropomyosin 1,
- NOTE Confidence: 0.833239409166667

 $00:47:25.390 \longrightarrow 00:47:26.702$ myosin light chain two.

NOTE Confidence: 0.833239409166667

 $00{:}47{:}26.702 \dashrightarrow 00{:}47{:}27.686$ Again there was.

NOTE Confidence: 0.833239409166667

00:47:27.690 --> 00:47:29.061 Very strong correlation

NOTE Confidence: 0.833239409166667

00:47:29.061 -> 00:47:30.889 collagens for fibroblasts and

NOTE Confidence: 0.833239409166667

 $00:47:30.889 \rightarrow 00:47:33.080$ hemoglobins for red blood cells.

NOTE Confidence: 0.833239409166667

 $00{:}47{:}33.080 \dashrightarrow 00{:}47{:}35.165$ So this method actually worked

NOTE Confidence: 0.833239409166667

00:47:35.165 --> 00:47:36.833 reasonably well at identifying

NOTE Confidence: 0.833239409166667

 $00:47:36.833 \longrightarrow 00:47:38.708$ what was present at each of

NOTE Confidence: 0.833239409166667

 $00{:}47{:}38.708 \dashrightarrow 00{:}47{:}40.860$ those cells and if we did a UMAP,

NOTE Confidence: 0.833239409166667

 $00:47:40.860 \longrightarrow 00:47:43.730$ which is a way of sort of

NOTE Confidence: 0.833239409166667

 $00:47:43.730 \longrightarrow 00:47:45.320$ structuring the data in.

NOTE Confidence: 0.833239409166667

00:47:45.320 --> 00:47:46.795 Kind of from A3 dimensional

NOTE Confidence: 0.833239409166667

 $00:47:46.795 \rightarrow 00:47:48.270$ where everything is located down

NOTE Confidence: 0.833239409166667

 $00{:}47{:}48.323 \dashrightarrow 00{:}47{:}49.748$ to two-dimensional structure.

NOTE Confidence: 0.833239409166667

 $00{:}47{:}49.750 \dashrightarrow 00{:}47{:}52.330$ You can see that this separated

NOTE Confidence: 0.833239409166667

 $00:47:52.330 \longrightarrow 00:47:54.050$ the myocarditis cases from

- NOTE Confidence: 0.833239409166667
- $00:47:54.130 \longrightarrow 00:47:56.058$ the non myocarditis cases.
- NOTE Confidence: 0.833239409166667
- $00:47:56.060 \rightarrow 00:47:57.200$ So the signal, the,
- NOTE Confidence: 0.833239409166667
- $00:47:57.200 \rightarrow 00:47:59.239$ the question we were asking though is
- NOTE Confidence: 0.833239409166667
- $00{:}47{:}59{.}239 \dashrightarrow 00{:}48{:}01{.}157$ can we see interesting signals at a
- NOTE Confidence: 0.833239409166667
- $00:48:01.157 \rightarrow 00:48:02.980$ distance from the inflammatory cells?
- NOTE Confidence: 0.833239409166667
- $00:48:02.980 \longrightarrow 00:48:04.793$ Can we pick up something that the
- NOTE Confidence: 0.833239409166667
- 00:48:04.793 --> 00:48:06.320 myocytes next door are screaming,
- NOTE Confidence: 0.833239409166667
- $00:48:06.320 \longrightarrow 00:48:07.060$ hey, hey,
- NOTE Confidence: 0.833239409166667
- $00:48:07.060 \longrightarrow 00:48:08.540$ I'm seeing there's this
- NOTE Confidence: 0.833239409166667
- $00:48:08.540 \rightarrow 00:48:10.400$ inflammation going on over here.
- NOTE Confidence: 0.833239409166667
- $00:48:10.400 \rightarrow 00:48:12.900$ And so this is just a little bit of data.
- NOTE Confidence: 0.833239409166667
- 00:48:12.900 --> 00:48:14.514 My buddy Luigi thinks he's going
- NOTE Confidence: 0.833239409166667
- $00{:}48{:}14{.}514 \dashrightarrow 00{:}48{:}16{.}400$ to make a company make millions.
- NOTE Confidence: 0.833239409166667
- 00:48:16.400 --> 00:48:17.324 I don't think so.
- NOTE Confidence: 0.833239409166667
- 00:48:17.324 --> 00:48:19.396 But I told him I wouldn't tell him what
- NOTE Confidence: 0.833239409166667

00:48:19.396 - 00:48:21.460 a gene name was and so he was happy.

NOTE Confidence: 0.833239409166667

 $00{:}48{:}21{.}460 \dashrightarrow 00{:}48{:}23{.}914$ So this is an example of

NOTE Confidence: 0.833239409166667

 $00:48:23.914 \longrightarrow 00:48:25.550$ of what we're seeing.

NOTE Confidence: 0.833239409166667

 $00:48:25.550 \rightarrow 00:48:27.503$ This is a collection of immune cells

NOTE Confidence: 0.833239409166667

 $00:48:27.503 \longrightarrow 00:48:29.580$ right here on the edge of a biopsy.

NOTE Confidence: 0.833239409166667

 $00{:}48{:}29{.}580 \dashrightarrow 00{:}48{:}31{.}235$ And you'll note there's not

NOTE Confidence: 0.833239409166667

00:48:31.235 --> 00:48:33.300 a blue or Gray signal here.

NOTE Confidence: 0.833239409166667

 $00:48:33.300 \rightarrow 00:48:36.184$ What we've done is we've removed any

NOTE Confidence: 0.833239409166667

00:48:36.184 --> 00:48:40.516 location that had CD 45 positivity or PT PRC.

NOTE Confidence: 0.833239409166667

 $00:48:40.520 \rightarrow 00:48:42.616$ CD 45 is a pan immune cell marker.

NOTE Confidence: 0.833239409166667

 $00:48:42.620 \longrightarrow 00:48:45.374$ So we said let's ignore anywhere

NOTE Confidence: 0.833239409166667

 $00:48:45.374 \longrightarrow 00:48:47.710$ where there's an immune cell.

NOTE Confidence: 0.833239409166667

 $00:48:47.710 \longrightarrow 00:48:50.170$ Then let's see what is present

NOTE Confidence: 0.833239409166667

 $00:48:50.170 \longrightarrow 00:48:53.296$ in myocarditis samples.

NOTE Confidence: 0.833239409166667

00:48:53.296 --> 00:48:55.380 In nonimmune.

NOTE Confidence: 0.833239409166667

00:48:55.380 --> 00:48:56.990 Help.

- NOTE Confidence: 0.833239409166667
- $00:48:56.990 \longrightarrow 00:48:59.910$ Whole of one of the genes that was
- NOTE Confidence: 0.833239409166667
- $00{:}48{:}59{.}910 \dashrightarrow 00{:}49{:}02{.}000$ identified where each one of these
- NOTE Confidence: 0.833239409166667
- $00:49:02.000 \rightarrow 00:49:04.720$ blue dots has a signal from that gene.
- NOTE Confidence: 0.833239409166667
- 00:49:04.720 --> 00:49:06.764 And every Gray area is a place
- NOTE Confidence: 0.833239409166667
- $00:49:06.764 \rightarrow 00:49:09.054$ where it doesn't and you can see
- NOTE Confidence: 0.833239409166667
- 00:49:09.054 --> 00:49:10.398 across this myocarditis biopsy
- NOTE Confidence: 0.833239409166667
- $00:49:10.398 \longrightarrow 00:49:12.691$ we have lots and lots of these
- NOTE Confidence: 0.833239409166667
- $00:49:12.691 \longrightarrow 00:49:14.786$ blue signals versus here on this
- NOTE Confidence: 0.833239409166667
- $00:49:14.786 \longrightarrow 00:49:17.466$ non myocarditis case we have
- NOTE Confidence: 0.833239409166667
- 00:49:17.466 --> 00:49:19.731 almost no CD 45 positivity.
- NOTE Confidence: 0.833239409166667
- $00:49:19.731 \longrightarrow 00:49:22.510$ We immune cells are rare in normal
- NOTE Confidence: 0.833239409166667
- $00:49:22.595 \rightarrow 00:49:25.301$ heart although they are present and
- NOTE Confidence: 0.833239409166667
- $00:49:25.301 \rightarrow 00:49:28.178$ just an occasional spot of this blue.
- NOTE Confidence: 0.833239409166667
- $00{:}49{:}28.180 \dashrightarrow 00{:}49{:}30.172$ So that to me is is pretty optimistic
- NOTE Confidence: 0.833239409166667
- $00{:}49{:}30{.}172 \dashrightarrow 00{:}49{:}32{.}344$ that we are seeing signals coming from
- NOTE Confidence: 0.833239409166667

 $00:49:32.344 \longrightarrow 00:49:34.690$ non immune cells that could be doing

NOTE Confidence: 0.833239409166667

 $00{:}49{:}34{.}690 \dashrightarrow 00{:}49{:}36{.}730$ exactly what we're hoping for signaling.

NOTE Confidence: 0.833239409166667

 $00:49:36.730 \longrightarrow 00:49:39.850$ That inflammation is nearby.

NOTE Confidence: 0.833239409166667

00:49:39.850 - 00:49:42.050 This is a more recently I was able to

NOTE Confidence: 0.833239409166667

 $00:49:42.110 \rightarrow 00:49:44.366$ look at a case of a chronic myocarditis,

NOTE Confidence: 0.833239409166667

 $00{:}49{:}44{.}370 \dashrightarrow 00{:}49{:}46{.}806$ lots of immune cells but without

NOTE Confidence: 0.833239409166667

 $00:49:46.806 \longrightarrow 00:49:48.430$ myocyte inflammation from a

NOTE Confidence: 0.833239409166667

 $00:49:48.498 \longrightarrow 00:49:50.188$ a larger chunk of tissue.

NOTE Confidence: 0.833239409166667

 $00{:}49{:}50{.}190 \dashrightarrow 00{:}49{:}52{.}826$ And here again this is CD45 which

NOTE Confidence: 0.833239409166667

 $00:49:52.826 \longrightarrow 00:49:54.866$ are these cells right here.

NOTE Confidence: 0.833239409166667

 $00:49:54.870 \longrightarrow 00:49:57.230$ The adipocytes in this location

NOTE Confidence: 0.833239409166667

 $00:49:57.230 \longrightarrow 00:49:59.590$ are this stream right along

NOTE Confidence: 0.833239409166667

00:49:59.677 - 00:50:02.078 the side and so where you see.

NOTE Confidence: 0.833239409166667

 $00:50:02.080 \longrightarrow 00:50:04.048$ There are are.

NOTE Confidence: 0.802991209090909

 $00{:}50{:}09{.}270 \dashrightarrow 00{:}50{:}11{.}178$ The first was that there was

NOTE Confidence: 0.802991209090909

 $00:50:11.178 \rightarrow 00:50:13.120$ actually like a negative biomarker.

00:50:16.340 --> 00:50:17.672 Have reasonable expression

NOTE Confidence: 0.771345498571429

 $00:50:17.672 \longrightarrow 00:50:19.448$ levels of this marker.

NOTE Confidence: 0.771345498571429

 $00:50:19.450 \longrightarrow 00:50:21.736$ And then as we got closer to the immune

NOTE Confidence: 0.771345498571429

 $00:50:21.736 \rightarrow 00:50:23.186$ infiltrate, which was over here,

NOTE Confidence: 0.771345498571429

 $00{:}50{:}23.186 \dashrightarrow 00{:}50{:}25.873$ we started to see less of that biomarker

NOTE Confidence: 0.771345498571429

 $00:50:25.873 \rightarrow 00:50:28.357$ and we also had positive biomarkers.

NOTE Confidence: 0.771345498571429

00:50:28.360 --> 00:50:30.200 So again, CD45 represents

NOTE Confidence: 0.771345498571429

 $00:50:30.200 \longrightarrow 00:50:32.040$ all the immune cells.

NOTE Confidence: 0.771345498571429

 $00{:}50{:}32.040 \dashrightarrow 00{:}50{:}34.418$ If we go beyond that, you start to

NOTE Confidence: 0.771345498571429

 $00:50:34.418 \rightarrow 00:50:36.398$ seeing there's more signal there.

NOTE Confidence: 0.771345498571429

 $00{:}50{:}36{.}400 \dashrightarrow 00{:}50{:}38{.}284$ So we are somewhat optimistic we

NOTE Confidence: 0.771345498571429

 $00{:}50{:}38{.}284 \dashrightarrow 00{:}50{:}40{.}683$ might be able to find something that

NOTE Confidence: 0.771345498571429

00:50:40.683 --> 00:50:43.196 will extend out from areas of injury

NOTE Confidence: 0.771345498571429

 $00{:}50{:}43.260 \dashrightarrow 00{:}50{:}45.440$ and that can identify myocarditis.

NOTE Confidence: 0.771345498571429

 $00{:}50{:}45{.}440 \dashrightarrow 00{:}50{:}46{.}472$ And I'll add that we're not

 $00:50:46.472 \longrightarrow 00:50:47.380$ the only people doing this,

NOTE Confidence: 0.771345498571429

 $00:50:47.380 \longrightarrow 00:50:47.989$ I've already heard.

NOTE Confidence: 0.771345498571429

 $00{:}50{:}47{.}989 \dashrightarrow 00{:}50{:}49{.}840$ Of lots of other groups have had this idea.

NOTE Confidence: 0.771345498571429

 $00:50:49.840 \longrightarrow 00:50:50.938$ I don't think we're that clever.

NOTE Confidence: 0.79585944

 $00{:}50{:}55{.}080 \dashrightarrow 00{:}50{:}56{.}280$ But as I said before,

NOTE Confidence: 0.79585944

 $00:50:56.280 \rightarrow 00:50:58.260$ the goals are to identify biomarkers

NOTE Confidence: 0.79585944

 $00{:}50{:}58{.}260 \dashrightarrow 00{:}51{:}00{.}899$ or a biomarker that can be used to

NOTE Confidence: 0.79585944

 $00:51:00.899 \rightarrow 00:51:02.464$ diagnose myocarditis in the absence

NOTE Confidence: 0.79585944

00:51:02.464 --> 00:51:04.437 of inflammation or myocyte injury

NOTE Confidence: 0.79585944

 $00{:}51{:}04{.}437 \dashrightarrow 00{:}51{:}06{.}437$ in the right clinical setting.

NOTE Confidence: 0.79585944

 $00{:}51{:}06{.}440 \dashrightarrow 00{:}51{:}09{.}038$ And ultimately the goal is to

NOTE Confidence: 0.79585944

 $00:51:09.038 \rightarrow 00:51:11.970$ increase the yield on our biopsies.

NOTE Confidence: 0.79585944

00:51:11.970 --> 00:51:14.708 So I'm going to end things now and

NOTE Confidence: 0.79585944

 $00:51:14.708 \rightarrow 00:51:17.046$ give you a few take home messages.

NOTE Confidence: 0.79585944

00:51:17.050 --> 00:51:19.468 There are challenges as I said,

NOTE Confidence: 0.79585944

 $00:51:19.470 \longrightarrow 00:51:21.262$ how to diagnose myocarditis

- NOTE Confidence: 0.79585944
- $00{:}51{:}21{.}262 \dashrightarrow 00{:}51{:}25{.}253$ in 2022 remains in. Oh.

 $00:51:25.253 \rightarrow 00:51:27.868$ Don't have a great way

NOTE Confidence: 0.79585944

 $00:51:27.868 \longrightarrow 00:51:29.960$ of making the diagnosis.

NOTE Confidence: 0.79585944

 $00{:}51{:}29{.}960 \dashrightarrow 00{:}51{:}31{.}600$ Biopsying which has historically

NOTE Confidence: 0.79585944

 $00:51:31.600 \longrightarrow 00:51:33.650$ been called the gold standard

NOTE Confidence: 0.79585944

 $00:51:33.650 \longrightarrow 00:51:35.471$ is plagued by inconsistencies

NOTE Confidence: 0.79585944

00:51:35.471 -> 00:51:37.716 how we approach the diagnosis,

NOTE Confidence: 0.79585944

 $00:51:37.720 \longrightarrow 00:51:39.750$ whether we can agree on the diagnosis

NOTE Confidence: 0.79585944

 $00{:}51{:}39{.}750 \dashrightarrow 00{:}51{:}41{.}616$ and whether we can even see the

NOTE Confidence: 0.79585944

 $00{:}51{:}41.616 \dashrightarrow 00{:}51{:}43.640$ areas we need to make the diagnosis.

NOTE Confidence: 0.79585944

 $00{:}51{:}43.640 \dashrightarrow 00{:}51{:}45.065$ But there are also opportunities

NOTE Confidence: 0.79585944

 $00{:}51{:}45.065 \dashrightarrow 00{:}51{:}47.339$ we are going to be working towards

NOTE Confidence: 0.79585944

00:51:47.339 --> 00:51:49.299 improved and new myocarditis criteria

NOTE Confidence: 0.79585944

 $00{:}51{:}49{.}299 \dashrightarrow 00{:}51{:}51{.}173$ for biopsies and whole hearts

NOTE Confidence: 0.79585944

 $00:51:51.173 \rightarrow 00:51:53.087$ which should improve the way we

 $00:51:53.087 \rightarrow 00:51:55.550$ approach the biopsies and we think

NOTE Confidence: 0.79585944

 $00:51:55.550 \rightarrow 00:51:57.825$ that non immune cell signaling.

NOTE Confidence: 0.79585944

 $00{:}51{:}57{.}830$ --> $00{:}52{:}00{.}956$ On biopsy can indicate myocarditis occurring NOTE Confidence: 0.79585944

 $00:52:00.956 \dashrightarrow 00:52:05.097$ even if we can't see those immune cells.

NOTE Confidence: 0.79585944

 $00{:}52{:}05{.}100 \dashrightarrow 00{:}52{:}07{.}130$ So I want to thank Zen Liu for the work

NOTE Confidence: 0.79585944

 $00{:}52{:}07{.}191 \dashrightarrow 00{:}52{:}09{.}223$ he did when we worked with our experts, NOTE Confidence: 0.79585944

00:52:09.230 --> 00:52:11.430 Luigi and Kevin on the last part of

NOTE Confidence: 0.79585944

 $00:52:11.430 \rightarrow 00:52:13.198$ this with the spatial transcriptomics

NOTE Confidence: 0.79585944

 $00{:}52{:}13.198 \dashrightarrow 00{:}52{:}15.893$ and then members of our society and NOTE Confidence: 0.79585944

00:52:15.957 --> 00:52:17.882 the European Society for working

NOTE Confidence: 0.79585944

 $00{:}52{:}17.882 \dashrightarrow 00{:}52{:}19.807$ to update and create criteria.

NOTE Confidence: 0.79585944

 $00:52:19.810 \longrightarrow 00:52:21.231$ And I'll end there and I'm happy

NOTE Confidence: 0.79585944

 $00{:}52{:}21{.}231 \dashrightarrow 00{:}52{:}22{.}720$ to take any of your questions.

NOTE Confidence: 0.5214029

 $00{:}52{:}31{.}690 \dashrightarrow 00{:}52{:}34{.}020$ This question. Yeah.

NOTE Confidence: 0.63493805

 $00{:}52{:}36{.}480 \dashrightarrow 00{:}52{:}36{.}980$ Look at.

NOTE Confidence: 0.9188627

 $00:52:43.230 \longrightarrow 00:52:45.666$ Yeah. So the the question from home,

- NOTE Confidence: 0.794872648
- 00:52:45.670 --> 00:52:46.678 if I make sure I'm getting

 $00:52:46.678 \rightarrow 00:52:47.350$ this right as well,

NOTE Confidence: 0.794872648

 $00:52:47.350 \longrightarrow 00:52:50.982$ is people looked at CD3 and how that

NOTE Confidence: 0.794872648

 $00:52:50.982 \rightarrow 00:52:54.888$ relates to steroid use immunosuppression.

NOTE Confidence: 0.794872648

 $00{:}52{:}54{.}890 \dashrightarrow 00{:}52{:}57{.}210$ So I don't know that I've seen that.

NOTE Confidence: 0.794872648

 $00:52:57.210 \longrightarrow 00:52:58.730$ I haven't done that,

NOTE Confidence: 0.794872648

 $00:52:58.730 \longrightarrow 00:53:01.010$ I'll tell you that right now.

NOTE Confidence: 0.794872648

 $00:53:01.010 \longrightarrow 00:53:02.630$ And I have to look there,

NOTE Confidence: 0.794872648

 $00:53:02.630 \longrightarrow 00:53:04.240$ that's going to be one of the

NOTE Confidence: 0.794872648

 $00:53:04.240 \rightarrow 00:53:05.439$ huge challenges that we're going

NOTE Confidence: 0.794872648

 $00{:}53{:}05{.}439 \dashrightarrow 00{:}53{:}07{.}049$ to face when we try and evaluate

NOTE Confidence: 0.794872648

 $00{:}53{:}07{.}049 \dashrightarrow 00{:}53{:}08{.}707$ these is what are the different

NOTE Confidence: 0.794872648

 $00:53:08.707 \dashrightarrow 00:53:10.087$ treatments that patients have had,

NOTE Confidence: 0.794872648

00:53:10.090 --> 00:53:11.845 because that's going to impact

NOTE Confidence: 0.794872648

 $00:53:11.845 \longrightarrow 00:53:13.535$ on outcome as well, right.

 $00:53:13.535 \rightarrow 00:53:15.815$ So normally at a time of biopsy early

NOTE Confidence: 0.794872648

 $00:53:15.815 \rightarrow 00:53:18.308$ when we're diagnosed as acute myocarditis,

NOTE Confidence: 0.794872648

 $00:53:18.310 \longrightarrow 00:53:19.090$ they haven't necessarily

NOTE Confidence: 0.794872648

 $00:53:19.090 \rightarrow 00:53:20.390$ gone on a treatment yet.

NOTE Confidence: 0.794872648

 $00:53:20.390 \rightarrow 00:53:23.846$ So what we see is really more natively

NOTE Confidence: 0.794872648

 $00:53:23.846 \rightarrow 00:53:25.820$ what's happening in the heart.

NOTE Confidence: 0.794872648

 $00{:}53{:}25{.}820 \dashrightarrow 00{:}53{:}27{.}872$ So we could see the full

NOTE Confidence: 0.794872648

00:53:27.872 --> 00:53:29.240 gamut of inflammation there,

NOTE Confidence: 0.794872648

00:53:29.240 --> 00:53:32.222 but the question is if different practices

NOTE Confidence: 0.794872648

 $00{:}53{:}32{.}222 \dashrightarrow 00{:}53{:}34{.}325$ and different institutions treat with

NOTE Confidence: 0.794872648

 $00{:}53{:}34{.}325 \dashrightarrow 00{:}53{:}36{.}593$ steroids or don't treat with steroids,

NOTE Confidence: 0.794872648

 $00:53:36.600 \rightarrow 00:53:39.360$ how do we figure that out for outcome?

NOTE Confidence: 0.794872648

 $00{:}53{:}39{.}360 \dashrightarrow 00{:}53{:}41{.}138$ And that's a good question as well.

NOTE Confidence: 0.794872648

00:53:41.140 --> 00:53:43.390 And that's going to be very hard to do

NOTE Confidence: 0.794872648

 $00{:}53{:}43{.}390 \dashrightarrow 00{:}53{:}45{.}407$ where we're going to look at different

NOTE Confidence: 0.794872648

 $00:53:45.407 \rightarrow 00:53:47.518$ data sets and and figure that out.

- NOTE Confidence: 0.794872648
- 00:53:47.520 --> 00:53:49.370 Second question,
- NOTE Confidence: 0.794872648
- $00:53:49.370 \longrightarrow 00:53:49.870$ yes.
- NOTE Confidence: 0.543855205
- $00:53:51.420 \rightarrow 00:53:54.180$ That was something against
- NOTE Confidence: 0.543855205
- $00:53:54.180 \rightarrow 00:53:56.590$ what people think or.
- NOTE Confidence: 0.871884275714286
- 00:53:57.770 --> 00:54:01.250 Yeah, I, I I don't remember anymore. I.
- NOTE Confidence: 0.18045843
- $00{:}54{:}16.260 \dashrightarrow 00{:}54{:}16.750$ Today.
- NOTE Confidence: 0.687088440714286
- $00:54:21.190 \rightarrow 00:54:26.182$ My question is how expanded would be these
- NOTE Confidence: 0.687088440714286
- $00:54:26.182 \rightarrow 00:54:30.177$ changes around the areas or permission?
- NOTE Confidence: 0.687088440714286
- $00{:}54{:}30{.}180 \dashrightarrow 00{:}54{:}32{.}310$ Because if it is really expanded
- NOTE Confidence: 0.687088440714286
- $00:54:32.310 \longrightarrow 00:54:34.530$ then you would have a higher
- NOTE Confidence: 0.687088440714286
- $00:54:34.530 \longrightarrow 00:54:36.335$ chance of violating for each
- NOTE Confidence: 0.687088440714286
- $00:54:36.340 \longrightarrow 00:54:40.740$ and every other piece but.
- NOTE Confidence: 0.687088440714286
- $00{:}54{:}40{.}740 \dashrightarrow 00{:}54{:}43{.}210$ Yeah, and you will stop.
- NOTE Confidence: 0.687088440714286
- $00{:}54{:}43{.}210 \dashrightarrow 00{:}54{:}44{.}706$ Basically the same time
- NOTE Confidence: 0.687088440714286
- $00{:}54{:}44{.}706 \dashrightarrow 00{:}54{:}46{.}576$ concept of meeting the area.
- NOTE Confidence: 0.804246022857143

 $00{:}54{:}47{.}930 \dashrightarrow 00{:}54{:}50{.}642$ Yeah, you, you exactly elucidate the

NOTE Confidence: 0.804246022857143

 $00:54:50.642 \longrightarrow 00:54:53.807$ the question that we have no idea of,

NOTE Confidence: 0.804246022857143

 $00:54:53.810 \longrightarrow 00:54:56.802$ which is how far out will that signal

NOTE Confidence: 0.804246022857143

 $00:54:56.802 \rightarrow 00:54:58.609$ extend relative to the biopsy.

NOTE Confidence: 0.804246022857143

 $00:54:58.610 \rightarrow 00:55:00.866$ And the longer, the further out it goes,

NOTE Confidence: 0.804246022857143

 $00:55:00.870 \rightarrow 00:55:02.676$ the more successful this is going

NOTE Confidence: 0.804246022857143

 $00:55:02.676 \dashrightarrow 00:55:05.228$ to be and the less it extends out,

NOTE Confidence: 0.804246022857143

 $00:55:05.230 \rightarrow 00:55:06.749$ the less successful it's going to be.

NOTE Confidence: 0.804246022857143

 $00{:}55{:}06.750 \dashrightarrow 00{:}55{:}09.945$ And we've only shown we've only done this on.

NOTE Confidence: 0.804246022857143

 $00:55:09.950 \longrightarrow 00:55:11.678$ 5 myocarditis cases for

NOTE Confidence: 0.804246022857143

 $00{:}55{:}11.678$ --> $00{:}55{:}13.406$ acute and one chronic.

NOTE Confidence: 0.804246022857143

 $00:55:13.410 \rightarrow 00:55:16.110$ We've put in some grants to try and get many,

NOTE Confidence: 0.804246022857143

 $00:55:16.110 \longrightarrow 00:55:17.840$ many more cases and find

NOTE Confidence: 0.804246022857143

 $00:55:17.840 \longrightarrow 00:55:19.570$ the markers that have the,

NOTE Confidence: 0.804246022857143

 $00{:}55{:}19{.}570 \dashrightarrow 00{:}55{:}22{.}244$ the sort of the widest capture area.

NOTE Confidence: 0.804246022857143

 $00:55:22.250 \rightarrow 00:55:23.734$ And that's going to be absolutely critical.

- NOTE Confidence: 0.804246022857143
- 00:55:23.740 --> 00:55:25.126 And if we don't find anything,
- NOTE Confidence: 0.804246022857143
- $00:55:25.130 \rightarrow 00:55:26.738$ this obviously won't work.
- NOTE Confidence: 0.804246022857143
- $00:55:26.738 \longrightarrow 00:55:28.642$ So high risk, high reward,
- NOTE Confidence: 0.804246022857143
- $00:55:28.642 \rightarrow 00:55:31.064$ but if we can't extend that out,
- NOTE Confidence: 0.804246022857143
- $00:55:31.070 \longrightarrow 00:55:32.335$ we're going to be able
- NOTE Confidence: 0.804246022857143
- $00:55:32.335 \longrightarrow 00:55:33.347$ to make more diagnosis.
- NOTE Confidence: 0.804246022857143
- $00{:}55{:}33{.}350 \dashrightarrow 00{:}55{:}34{.}771$ And I think that's a great thing
- NOTE Confidence: 0.804246022857143
- 00:55:34.771 > 00:55:36.219 that we can make that happen.
- NOTE Confidence: 0.8564615
- 00:55:38.960 --> 00:55:42.798 So I just. Questions why is the?
- NOTE Confidence: 0.646198923333333
- $00:55:48.640 \rightarrow 00:55:50.050$ So that and we stop typing.
- NOTE Confidence: 0.23320433
- $00:55:52.130 \longrightarrow 00:55:52.680$ Tell.
- NOTE Confidence: 0.42452544
- $00{:}55{:}55{.}220 \dashrightarrow 00{:}55{:}55{.}600$ Weather.
- NOTE Confidence: 0.95544696
- $00{:}55{:}58{.}820 \dashrightarrow 00{:}56{:}00{.}860$ Yeah, so that's a great question.
- NOTE Confidence: 0.741508418333333
- $00:56:00.860 \longrightarrow 00:56:03.830$ Do we do subtyping of CD3?
- NOTE Confidence: 0.741508418333333
- $00{:}56{:}03.830 \dashrightarrow 00{:}56{:}06.310$ We do not. So one of the the I think
- NOTE Confidence: 0.741508418333333

 $00:56:06.384 \rightarrow 00:56:08.316$ challenges in the cardiovascular

NOTE Confidence: 0.741508418333333

 $00:56:08.316 \rightarrow 00:56:11.510$ pathology space is that we have not

NOTE Confidence: 0.741508418333333

 $00{:}56{:}11{.}510 \dashrightarrow 00{:}56{:}14{.}450$ really kept up in our field with.

NOTE Confidence: 0.741508418333333

 $00:56:14.450 \rightarrow 00:56:16.490$ Things like this like subtyping CD3

NOTE Confidence: 0.741508418333333

 $00{:}56{:}16.490 \dashrightarrow 00{:}56{:}19.359$ cells I on the research side it may

NOTE Confidence: 0.741508418333333

 $00{:}56{:}19{.}359 \dashrightarrow 00{:}56{:}21{.}989$ have happened but most people in the

NOTE Confidence: 0.741508418333333

00:56:21.989 --> 00:56:24.761 cardiovascular space just use CD3 and CD68.

NOTE Confidence: 0.741508418333333

 $00:56:24.761 \longrightarrow 00:56:27.428$ In fact this came up last week

NOTE Confidence: 0.741508418333333

 $00:56:27.430 \longrightarrow 00:56:29.056$ when Peter had a journal club.

NOTE Confidence: 0.741508418333333

 $00{:}56{:}29.060 \dashrightarrow 00{:}56{:}31.811$ When we're talking about C 68 positive

NOTE Confidence: 0.741508418333333

 $00{:}56{:}31{.}811 \dashrightarrow 00{:}56{:}33{.}720$ cells were being increased seen in

NOTE Confidence: 0.741508418333333

00:56:33.720 --> 00:56:35.563 COVID and our colleague Jeff Zaffis

NOTE Confidence: 0.741508418333333

 $00:56:35.563 \longrightarrow 00:56:37.488$ was arguing that it's it's silly to

NOTE Confidence: 0.741508418333333

 $00:56:37.488 \longrightarrow 00:56:39.920$ just look at CD 68 that we have to

NOTE Confidence: 0.741508418333333

 $00:56:39.920 \rightarrow 00:56:41.238$ sub classify macrophages because we

NOTE Confidence: 0.741508418333333

 $00:56:41.238 \rightarrow 00:56:42.852$ know there's so many phenotypes of

 $00:56:42.852 \rightarrow 00:56:44.358$ macrophages that's really meaningful but.

NOTE Confidence: 0.741508418333333

 $00:56:44.360 \longrightarrow 00:56:46.264$ They don't have the tool to do that

NOTE Confidence: 0.741508418333333

 $00:56:46.264 \rightarrow 00:56:48.509$ and we just haven't implemented them.

NOTE Confidence: 0.741508418333333

 $00:56:48.510 \rightarrow 00:56:51.390$ So we don't go beyond CD3.

NOTE Confidence: 0.741508418333333

 $00:56:51.390 \longrightarrow 00:56:51.974$ Should we?

NOTE Confidence: 0.741508418333333

 $00{:}56{:}51{.}974 \dashrightarrow 00{:}56{:}54{.}018$ Yes, I mentioned TH 17 cells seem

NOTE Confidence: 0.741508418333333

00:56:54.018 - > 00:56:55.790 to be important in myocarditis

NOTE Confidence: 0.741508418333333

 $00:56:55.790 \longrightarrow 00:56:57.914$ and we are not doing anything

NOTE Confidence: 0.741508418333333

 $00:56:57.980 \longrightarrow 00:57:00.278$ clinically to chase that down either.

NOTE Confidence: 0.2796874

00:57:04.990 --> 00:57:05.680 Exactly.

NOTE Confidence: 0.659317546363636

00:57:10.430 --> 00:57:13.088 And ideas? So only small factory

NOTE Confidence: 0.659317546363636

 $00{:}57{:}13.088 \dashrightarrow 00{:}57{:}15.370$ of people would have this.

NOTE Confidence: 0.7805282166666667

 $00{:}57{:}20.730 \dashrightarrow 00{:}57{:}23.370$ So once you know what possible,

NOTE Confidence: 0.7805282166666667

 $00{:}57{:}23.370 \dashrightarrow 00{:}57{:}25.770$ you know what you think is

NOTE Confidence: 0.7805282166666667

 $00{:}57{:}25{.}770 \dashrightarrow 00{:}57{:}28{.}828$ underlying, you know, facts.

- $00:57:28.830 \longrightarrow 00:57:32.468$ This small. Right, so you know.
- NOTE Confidence: 0.48627472
- $00{:}57{:}34{.}530 \dashrightarrow 00{:}57{:}34{.}860$ Out.
- NOTE Confidence: 0.741980668571429
- $00:57:36.540 \rightarrow 00:57:38.804$ Got it. Yeah. So the question is why
- NOTE Confidence: 0.741980668571429
- $00:57:38.804 \rightarrow 00:57:41.057$ does these small group have Microsoft?
- NOTE Confidence: 0.741980668571429
- 00:57:41.060 --> 00:57:42.210 I thought you were gonna ask, well,
- NOTE Confidence: 0.741980668571429
- $00:57:42.210 \rightarrow 00:57:43.820$ why are so many people have cardiac
- NOTE Confidence: 0.741980668571429
- 00:57:43.820 --> 00:57:44.800 symptoms without myocarditis,
- NOTE Confidence: 0.741980668571429
- $00:57:44.800 \longrightarrow 00:57:46.180$ which to me is easier.
- NOTE Confidence: 0.741980668571429
- $00:57:46.180 \rightarrow 00:57:49.060$ We're seeing small vessel a thrombi,
- NOTE Confidence: 0.741980668571429
- 00:57:49.060 00:57:50.736 microthrombi in in people.
- NOTE Confidence: 0.741980668571429
- $00:57:50.736 \rightarrow 00:57:52.831$ We're seeing increased macrophages in
- NOTE Confidence: 0.741980668571429
- $00:57:52.831 \rightarrow 00:57:55.479$ the hearts of multiple studies of that.
- NOTE Confidence: 0.741980668571429
- $00:57:55.480 \longrightarrow 00:57:57.080$ But that's not myocarditis,
- NOTE Confidence: 0.741980668571429
- $00:57:57.080 \rightarrow 00:57:58.680$ that's just other processes
- NOTE Confidence: 0.741980668571429
- $00:57:58.680 \longrightarrow 00:58:00.799$ that are affecting the heart.
- NOTE Confidence: 0.741980668571429
- $00:58:00.800 \rightarrow 00:58:02.540$ As far as this group,

 $00:58:02.540 \longrightarrow 00:58:06.334$ I don't know why this 2% I would argue.

NOTE Confidence: 0.741980668571429

00:58:06.334 --> 00:58:07.846 Genetics is partly involved.

NOTE Confidence: 0.741980668571429

00:58:07.850 --> 00:58:12.330 Someone's set up for this, possibly.

NOTE Confidence: 0.741980668571429

00:58:12.330 --> 00:58:13.770 Sort of an autoimmune process

NOTE Confidence: 0.741980668571429

 $00:58:13.770 \longrightarrow 00:58:15.550$ that can get going as well.

NOTE Confidence: 0.741980668571429

 $00{:}58{:}15{.}550 \dashrightarrow 00{:}58{:}18{.}042$ I have not kept up with the

NOTE Confidence: 0.741980668571429

 $00{:}58{:}18.042 \dashrightarrow 00{:}58{:}19.810$ basic science data on this.

NOTE Confidence: 0.741980668571429

 $00{:}58{:}19{.}810 \dashrightarrow 00{:}58{:}21{.}370$ I'm sure there is a,

NOTE Confidence: 0.741980668571429

 $00{:}58{:}21.370 \dashrightarrow 00{:}58{:}22.648$ I'm sure there's hundreds of papers.

NOTE Confidence: 0.741980668571429

 $00:58:22.650 \rightarrow 00:58:24.370$ Whether some of them are good or not,

NOTE Confidence: 0.741980668571429

 $00{:}58{:}24{.}370 \dashrightarrow 00{:}58{:}25{.}630$ I don't know either.

NOTE Confidence: 0.741980668571429

 $00{:}58{:}25.630 \dashrightarrow 00{:}58{:}28.010$ But what we do know from COVID,

NOTE Confidence: 0.741980668571429

 $00{:}58{:}28{.}010 \dashrightarrow 00{:}58{:}29{.}410$ having looked at lots of

NOTE Confidence: 0.741980668571429

00:58:29.410 --> 00:58:30.810 cases I'm sure Peter agrees,

NOTE Confidence: 0.741980668571429

 $00:58:30.810 \longrightarrow 00:58:32.688$ is we see lots of macrophages,

 $00:58:32.690 \rightarrow 00:58:35.000$ I even see more macrophages and people

NOTE Confidence: 0.741980668571429

 $00{:}58{:}35{.}000 \dashrightarrow 00{:}58{:}37{.}449$ have heart failure after getting a vaccine,

NOTE Confidence: 0.741980668571429

 $00{:}58{:}37{.}450 \dashrightarrow 00{:}58{:}39{.}452$ but it's not a classic myocarditis and

NOTE Confidence: 0.741980668571429

 $00:58:39.452 \rightarrow 00:58:40.934$ that's actually something that we're

NOTE Confidence: 0.741980668571429

 $00{:}58{:}40{.}934 \dashrightarrow 00{:}58{:}42{.}644$ thinking about with the Dallas criteria.

NOTE Confidence: 0.741980668571429

 $00{:}58{:}42.650 \dashrightarrow 00{:}58{:}43.787$ Is do we?

NOTE Confidence: 0.741980668571429

 $00:58:43.787 \rightarrow 00:58:46.440$ Discussed some of these rare types of

NOTE Confidence: 0.741980668571429

 $00:58:46.527 \rightarrow 00:58:48.987$ myocarditis and be provide criteria

NOTE Confidence: 0.741980668571429

 $00{:}58{:}48{.}987 \dashrightarrow 00{:}58{:}51{.}898$ that are more specific to them

NOTE Confidence: 0.741980668571429

 $00:58:51.898 \rightarrow 00:58:54.802$ such as if you see this many miles

NOTE Confidence: 0.741980668571429

 $00{:}58{:}54{.}802 \dashrightarrow 00{:}58{:}56{.}731$ sites and I've seen a ton of Maya

NOTE Confidence: 0.741980668571429

 $00:58:56.731 \rightarrow 00:58:58.757$ sites in a couple of these cases,

NOTE Confidence: 0.741980668571429

 $00:58:58.760 \longrightarrow 00:59:00.488$ but that's not typical for myocarditis

NOTE Confidence: 0.741980668571429

 $00:59:00.488 \rightarrow 00:59:02.070$ which is a lymphocytic disease.

NOTE Confidence: 0.741980668571429

 $00:59:02.070 \rightarrow 00:59:03.380$ We've always thought about whether

NOTE Confidence: 0.741980668571429

 $00:59:03.380 \longrightarrow 00:59:05.383$ or not that should be sufficient to

- NOTE Confidence: 0.741980668571429
- $00:59:05.383 \rightarrow 00:59:06.988$ make the diagnosis of myocarditis.
- NOTE Confidence: 0.741980668571429
- $00{:}59{:}06{.}990 \dashrightarrow 00{:}59{:}09{.}495$ So that's something that we're
- NOTE Confidence: 0.741980668571429
- $00:59:09.495 \longrightarrow 00:59:11.499$ working through as well.
- NOTE Confidence: 0.741980668571429
- $00{:}59{:}11{.}500 \dashrightarrow 00{:}59{:}12{.}090$ After that.
- NOTE Confidence: 0.53410596
- $00{:}59{:}16{.}950 \dashrightarrow 00{:}59{:}17{.}460$ Ohh.
- NOTE Confidence: 0.8311198
- $00{:}59{:}20{.}310 \dashrightarrow 00{:}59{:}21{.}999$ We have talked about smoking in
- NOTE Confidence: 0.8311198
- $00:59:21.999 \longrightarrow 00:59:24.297$ the smoking nut in the mice,
- NOTE Confidence: 0.68932998
- $00:59:24.310 \longrightarrow 00:59:26.870$ which they activate phase
- NOTE Confidence: 0.68932998
- $00:59:26.870 \longrightarrow 00:59:31.549$ two and one. So that made.
- NOTE Confidence: 0.6374205
- $00:59:33.870 \longrightarrow 00:59:34.150$ Now.
- NOTE Confidence: 0.011551678
- 00:59:37.840 --> 00:59:39.010 Subpopulation.
- NOTE Confidence: 0.7412228225
- $00{:}59{:}41.660 \dashrightarrow 00{:}59{:}42.580$ So that will be.
- NOTE Confidence: 0.614373583333333
- 00:59:46.300 --> 00:59:51.830 No, only one. Yeah, yeah, yeah.
- NOTE Confidence: 0.3847024
- $00{:}59{:}53{.}990 \dashrightarrow 00{:}59{:}54{.}350$ Favorite.
- NOTE Confidence: 0.881277718
- $01{:}00{:}02.760 \dashrightarrow 01{:}00{:}03.990$ You heard it here first.
- NOTE Confidence: 0.88967291

- 01:00:08.750 --> 01:00:10.948 Yeah. Super fresh. Thank you for sharing.
- NOTE Confidence: 0.85017335
- $01:00:12.940 \longrightarrow 01:00:13.160$ Yeah.
- NOTE Confidence: 0.92597055
- $01{:}00{:}16.460 \dashrightarrow 01{:}00{:}18.730$ Great. Well, with that, I think
- NOTE Confidence: 0.92597055
- $01:00:18.730 \longrightarrow 01:00:20.639$ I'll thank you all for your time.
- NOTE Confidence: 0.5658411066666667
- $01:00:20.640 \longrightarrow 01:00:23.100$ It's been wonderful. Thank you.
- NOTE Confidence: 0.6070799
- $01:00:27.610 \longrightarrow 01:00:28.740$ There was nothing in the chat.
- NOTE Confidence: 0.28563768
- $01{:}00{:}34{.}920 \dashrightarrow 01{:}00{:}36{.}786$ There's some studies in the machine learning.
- NOTE Confidence: 0.42934057
- $01:00:39.940 \longrightarrow 01:00:42.240$ Reason.