

WEBVTT

NOTE duration:"01:02:02"

NOTE recognizability:0.840

NOTE language:en-us

NOTE Confidence: 0.768176794444445

00:00:00.000 --> 00:00:02.796 Nelly, and for that really wonderful

NOTE Confidence: 0.768176794444445

00:00:02.796 --> 00:00:04.752 introduction and for a persistence

NOTE Confidence: 0.768176794444445

00:00:04.752 --> 00:00:06.960 in inviting me to to give this talk

NOTE Confidence: 0.768176794444445

00:00:07.019 --> 00:00:08.879 for the Department of Psychiatry.

NOTE Confidence: 0.768176794444445

00:00:08.880 --> 00:00:11.102 And this is a great honor, you know,

NOTE Confidence: 0.768176794444445

00:00:11.102 --> 00:00:13.290 I've been at Yale for 11 years and I

NOTE Confidence: 0.768176794444445

00:00:13.290 --> 00:00:15.522 over just the last year or two through

NOTE Confidence: 0.768176794444445

00:00:15.522 --> 00:00:16.931 interactions with Chris Pittenger

NOTE Confidence: 0.768176794444445

00:00:16.931 --> 00:00:18.721 and more interactions with other

NOTE Confidence: 0.768176794444445

00:00:18.721 --> 00:00:20.074 colleagues and psychiatry really,

NOTE Confidence: 0.768176794444445

00:00:20.074 --> 00:00:21.976 really realized what a missed opportunity

NOTE Confidence: 0.768176794444445

00:00:21.976 --> 00:00:23.859 that's being all this time for me to

NOTE Confidence: 0.768176794444445

00:00:23.859 --> 00:00:25.400 not interact more with your department.

NOTE Confidence: 0.768176794444445

00:00:25.400 --> 00:00:27.528 So again, I hope this is just the
NOTE Confidence: 0.768176794444445

00:00:27.528 --> 00:00:29.379 beginning of a long standing set
NOTE Confidence: 0.768176794444445

00:00:29.379 --> 00:00:31.257 of intersections that we can have,
NOTE Confidence: 0.768176794444445

00:00:31.260 --> 00:00:32.124 and I think.
NOTE Confidence: 0.768176794444445

00:00:32.124 --> 00:00:32.700 In particular,
NOTE Confidence: 0.768176794444445

00:00:32.700 --> 00:00:35.352 my research interests and my clinical
NOTE Confidence: 0.768176794444445

00:00:35.352 --> 00:00:37.120 interests are really intersecting
NOTE Confidence: 0.768176794444445

00:00:37.183 --> 00:00:39.384 with psychiatric disease, and again,
NOTE Confidence: 0.768176794444445

00:00:39.384 --> 00:00:40.994 the brain and the mind,
NOTE Confidence: 0.768176794444445

00:00:41.000 --> 00:00:42.904 both in terms of cognition but also in
NOTE Confidence: 0.768176794444445

00:00:42.904 --> 00:00:44.699 terms of mood disorders is something
NOTE Confidence: 0.768176794444445

00:00:44.699 --> 00:00:46.589 that's really relevant to my work.
NOTE Confidence: 0.768176794444445

00:00:46.590 --> 00:00:49.677 So as you heard from Professor O'Malley,
NOTE Confidence: 0.768176794444445

00:00:49.680 --> 00:00:51.556 I've been working for a long time
NOTE Confidence: 0.768176794444445

00:00:51.556 --> 00:00:53.410 studying the effects of HIV in the brain.
NOTE Confidence: 0.768176794444445

00:00:53.410 --> 00:00:55.570 And then of course, 2020,

NOTE Confidence: 0.768176794444445
00:00:55.570 --> 00:00:58.150 because we had this massive onslaught
NOTE Confidence: 0.768176794444445
00:00:58.150 --> 00:01:00.918 of concerns about the brain and COVID,
NOTE Confidence: 0.768176794444445
00:01:00.920 --> 00:01:02.985 this became an area that I've also.
NOTE Confidence: 0.768176794444445
00:01:02.990 --> 00:01:06.008 Started to investigate one thing.
NOTE Confidence: 0.768176794444445
00:01:06.008 --> 00:01:07.553 That's a really important part
NOTE Confidence: 0.768176794444445
00:01:07.553 --> 00:01:10.024 of my sort of portfolio is I'm a
NOTE Confidence: 0.768176794444445
00:01:10.024 --> 00:01:12.342 clinician and I see patients and so
NOTE Confidence: 0.768176794444445
00:01:12.342 --> 00:01:15.254 I'm going to talk about the issues
NOTE Confidence: 0.768176794444445
00:01:15.254 --> 00:01:19.040 of CNS effects of COVID-19 really,
NOTE Confidence: 0.768176794444445
00:01:19.040 --> 00:01:20.970 starting from a clinical perspective,
NOTE Confidence: 0.768176794444445
00:01:20.970 --> 00:01:22.824 and I think that I'm going to try to
NOTE Confidence: 0.768176794444445
00:01:22.824 --> 00:01:24.869 kind of go through what we've understood
NOTE Confidence: 0.768176794444445
00:01:24.869 --> 00:01:27.068 what we've learned over the last two years,
NOTE Confidence: 0.768176794444445
00:01:27.070 --> 00:01:27.912 and really,
NOTE Confidence: 0.768176794444445
00:01:27.912 --> 00:01:30.438 all of that begins with clinical
NOTE Confidence: 0.768176794444445

00:01:30.438 --> 00:01:32.362 observations and and, you know,
NOTE Confidence: 0.768176794444445

00:01:32.362 --> 00:01:33.460 people worldwide reports.
NOTE Confidence: 0.768176794444445

00:01:33.460 --> 00:01:34.996 Worldwide and then some of our
NOTE Confidence: 0.768176794444445

00:01:34.996 --> 00:01:36.320 own experience here at Yale.
NOTE Confidence: 0.768176794444445

00:01:36.320 --> 00:01:38.920 So I'm gonna I'm gonna anchor the talk
NOTE Confidence: 0.768176794444445

00:01:38.920 --> 00:01:41.550 and talking about the CNS sorts of
NOTE Confidence: 0.768176794444445

00:01:41.550 --> 00:01:43.465 clinical reports and acute COVID-19.
NOTE Confidence: 0.768176794444445

00:01:43.470 --> 00:01:45.129 I'm going to then talk about what's
NOTE Confidence: 0.768176794444445

00:01:45.129 --> 00:01:46.626 being learned over the last two
NOTE Confidence: 0.768176794444445

00:01:46.626 --> 00:01:47.856 years about the neuropathic genesis
NOTE Confidence: 0.768176794444445

00:01:47.856 --> 00:01:49.359 of that acute COVID infection.
NOTE Confidence: 0.768176794444445

00:01:49.360 --> 00:01:50.142 So really,
NOTE Confidence: 0.768176794444445

00:01:50.142 --> 00:01:52.488 what's happening in the brain and
NOTE Confidence: 0.768176794444445

00:01:52.488 --> 00:01:54.360 people during acute COVID-19?
NOTE Confidence: 0.768176794444445

00:01:54.360 --> 00:01:56.000 Primarily people who were pretty
NOTE Confidence: 0.768176794444445

00:01:56.000 --> 00:01:58.008 severely ill is where most of

NOTE Confidence: 0.768176794444445
00:01:58.008 --> 00:01:59.538 our information has come from,
NOTE Confidence: 0.768176794444445
00:01:59.540 --> 00:02:01.511 and this is going to be sort of the
NOTE Confidence: 0.768176794444445
00:02:01.511 --> 00:02:03.513 jumping off point for the rest of my talk,
NOTE Confidence: 0.768176794444445
00:02:03.520 --> 00:02:05.040 which is talking about.
NOTE Confidence: 0.768176794444445
00:02:05.040 --> 00:02:05.800 Nervous system,
NOTE Confidence: 0.768176794444445
00:02:05.800 --> 00:02:09.118 long COVID or post acute sequelae
NOTE Confidence: 0.768176794444445
00:02:09.118 --> 00:02:10.224 of COVID-19.
NOTE Confidence: 0.768176794444445
00:02:10.230 --> 00:02:11.742 So the first thing I'm going
NOTE Confidence: 0.768176794444445
00:02:11.742 --> 00:02:13.108 to describe is neurologic and
NOTE Confidence: 0.768176794444445
00:02:13.108 --> 00:02:14.628 psychiatric reports in acute COVID,
NOTE Confidence: 0.768176794444445
00:02:14.630 --> 00:02:17.006 and I think that we as a globe
NOTE Confidence: 0.768176794444445
00:02:17.006 --> 00:02:19.623 first heard about the concern that
NOTE Confidence: 0.768176794444445
00:02:19.623 --> 00:02:22.063 there might be quote neurologic
NOTE Confidence: 0.768176794444445
00:02:22.063 --> 00:02:23.870 manifestations and people with
NOTE Confidence: 0.768176794444445
00:02:23.870 --> 00:02:26.366 COVID-19 from this report from Wuhan,
NOTE Confidence: 0.768176794444445

00:02:26.370 --> 00:02:26.603 China,
NOTE Confidence: 0.768176794444445

00:02:26.603 --> 00:02:28.234 and this was from one of the
NOTE Confidence: 0.768176794444445

00:02:28.234 --> 00:02:29.160 major hospitals that had,
NOTE Confidence: 0.768176794444445

00:02:29.160 --> 00:02:29.952 you know,
NOTE Confidence: 0.768176794444445

00:02:29.952 --> 00:02:32.724 thousands and thousands of patients in the
NOTE Confidence: 0.768176794444445

00:02:32.724 --> 00:02:35.152 first wave and what emerged from this.
NOTE Confidence: 0.768176794444445

00:02:35.152 --> 00:02:37.270 This hospital experience and actually was
NOTE Confidence: 0.768176794444445

00:02:37.329 --> 00:02:39.450 originally a preprint in March of 2020,
NOTE Confidence: 0.768176794444445

00:02:39.450 --> 00:02:40.750 was this.
NOTE Confidence: 0.768176794444445

00:02:40.750 --> 00:02:42.050 Fairly generalized,
NOTE Confidence: 0.768176794444445

00:02:42.050 --> 00:02:45.300 very clinically based report suggesting
NOTE Confidence: 0.768176794444445

00:02:45.300 --> 00:02:48.338 that 36% of people who were hospitalized
NOTE Confidence: 0.768176794444445

00:02:48.338 --> 00:02:49.930 with laboratory confirmed COVID-19
NOTE Confidence: 0.768176794444445

00:02:49.995 --> 00:02:51.475 had neurologic manifestations of
NOTE Confidence: 0.768176794444445

00:02:51.475 --> 00:02:53.695 disease and what you'll see here
NOTE Confidence: 0.919579350416667

00:02:53.756 --> 00:02:55.180 under the nervous system.

NOTE Confidence: 0.919579350416667
00:02:55.180 --> 00:02:57.100 Symptoms in this table is that
NOTE Confidence: 0.919579350416667
00:02:57.100 --> 00:02:58.380 it's pretty broad definitions,
NOTE Confidence: 0.919579350416667
00:02:58.380 --> 00:03:00.075 so CNS conditions,
NOTE Confidence: 0.919579350416667
00:03:00.075 --> 00:03:02.335 including things like dizziness,
NOTE Confidence: 0.919579350416667
00:03:02.340 --> 00:03:04.232 headache, and her consciousness,
NOTE Confidence: 0.919579350416667
00:03:04.232 --> 00:03:07.070 acute with vascular disease or stroke,
NOTE Confidence: 0.919579350416667
00:03:07.070 --> 00:03:09.518 and then there were also changes in smell,
NOTE Confidence: 0.919579350416667
00:03:09.520 --> 00:03:10.990 taste, and vision which were
NOTE Confidence: 0.919579350416667
00:03:10.990 --> 00:03:11.872 considered peripheral nervous
NOTE Confidence: 0.919579350416667
00:03:11.872 --> 00:03:13.399 system and also skeletal muscle.
NOTE Confidence: 0.919579350416667
00:03:13.400 --> 00:03:15.992 Injury now this is the type of report that
NOTE Confidence: 0.919579350416667
00:03:15.992 --> 00:03:18.536 was available early on in the pandemic,
NOTE Confidence: 0.919579350416667
00:03:18.540 --> 00:03:20.120 primarily because research investigation
NOTE Confidence: 0.919579350416667
00:03:20.120 --> 00:03:22.095 of these patients wasn't possible.
NOTE Confidence: 0.919579350416667
00:03:22.100 --> 00:03:23.815 These hospitals were overwhelmed as
NOTE Confidence: 0.919579350416667

00:03:23.815 --> 00:03:26.719 we also were at Yale with just an
NOTE Confidence: 0.919579350416667

00:03:26.719 --> 00:03:28.589 onslaught of patients and research
NOTE Confidence: 0.919579350416667

00:03:28.589 --> 00:03:31.017 collection of samples or data or
NOTE Confidence: 0.919579350416667

00:03:31.017 --> 00:03:32.633 even neuroimaging was essentially
NOTE Confidence: 0.919579350416667

00:03:32.633 --> 00:03:34.761 not available in most patients
NOTE Confidence: 0.919579350416667

00:03:34.761 --> 00:03:36.509 because of infection concerns.
NOTE Confidence: 0.919579350416667

00:03:36.510 --> 00:03:38.344 But this was the first hint that
NOTE Confidence: 0.919579350416667

00:03:38.344 --> 00:03:40.358 there might be a neurologic concern,
NOTE Confidence: 0.919579350416667

00:03:40.360 --> 00:03:41.893 and I think one of the most
NOTE Confidence: 0.919579350416667

00:03:41.893 --> 00:03:43.142 important findings of this initial
NOTE Confidence: 0.919579350416667

00:03:43.142 --> 00:03:44.218 report was the finding.
NOTE Confidence: 0.919579350416667

00:03:44.220 --> 00:03:46.008 Some of the patients came to
NOTE Confidence: 0.919579350416667

00:03:46.010 --> 00:03:48.110 the hospital with an primarily
NOTE Confidence: 0.919579350416667

00:03:48.110 --> 00:03:49.370 in neurologic manifestation,
NOTE Confidence: 0.919579350416667

00:03:49.370 --> 00:03:51.380 as they're preventing presenting syndrome,
NOTE Confidence: 0.919579350416667

00:03:51.380 --> 00:03:53.258 so that was probably the first

NOTE Confidence: 0.919579350416667

00:03:53.258 --> 00:03:55.495 clue that COVID is not necessarily

NOTE Confidence: 0.919579350416667

00:03:55.495 --> 00:03:57.327 only a respiratory disease,

NOTE Confidence: 0.919579350416667

00:03:57.330 --> 00:04:00.494 but in fact also has an impact

NOTE Confidence: 0.919579350416667

00:04:00.494 --> 00:04:03.568 in other organ systems as well.

NOTE Confidence: 0.919579350416667

00:04:03.570 --> 00:04:05.271 And So what we were able to do here

NOTE Confidence: 0.919579350416667

00:04:05.271 --> 00:04:07.220 at Yale because we had this sort of

NOTE Confidence: 0.919579350416667

00:04:07.220 --> 00:04:09.073 warning ahead of time that there were

NOTE Confidence: 0.919579350416667

00:04:09.073 --> 00:04:11.230 concerns coming out of both China and Europe.

NOTE Confidence: 0.919579350416667

00:04:11.230 --> 00:04:13.754 And also when we sort of knew that the

NOTE Confidence: 0.919579350416667

00:04:13.754 --> 00:04:16.154 wave was coming in the beginning of March,

NOTE Confidence: 0.919579350416667

00:04:16.160 --> 00:04:17.816 we sort of scrambled to put

NOTE Confidence: 0.919579350416667

00:04:17.816 --> 00:04:19.702 together what we called a neuro

NOTE Confidence: 0.919579350416667

00:04:19.702 --> 00:04:21.146 COVID inpatient console service.

NOTE Confidence: 0.919579350416667

00:04:21.150 --> 00:04:22.692 And this was essentially me working

NOTE Confidence: 0.919579350416667

00:04:22.692 --> 00:04:24.770 with a couple of neurology residents,

NOTE Confidence: 0.919579350416667

00:04:24.770 --> 00:04:25.742 primarily Lindsey McAlpine
NOTE Confidence: 0.919579350416667

00:04:25.742 --> 00:04:27.686 shown up here on the right,
NOTE Confidence: 0.919579350416667

00:04:27.690 --> 00:04:29.594 but also to have a garden is
NOTE Confidence: 0.919579350416667

00:04:29.594 --> 00:04:31.259 also coming into your program,
NOTE Confidence: 0.919579350416667

00:04:31.260 --> 00:04:34.606 and we essentially were whenever there was.
NOTE Confidence: 0.919579350416667

00:04:34.610 --> 00:04:35.642 Inpatient neurology konsult
NOTE Confidence: 0.919579350416667

00:04:35.642 --> 00:04:38.050 on on someone who was known to
NOTE Confidence: 0.919579350416667

00:04:38.110 --> 00:04:39.890 have COVID-19 in the hospital.
NOTE Confidence: 0.919579350416667

00:04:39.890 --> 00:04:41.792 We essentially got involved in the
NOTE Confidence: 0.919579350416667

00:04:41.792 --> 00:04:43.730 consultation so we mostly did this
NOTE Confidence: 0.919579350416667

00:04:43.730 --> 00:04:45.260 through virtual chart reviews and
NOTE Confidence: 0.919579350416667

00:04:45.260 --> 00:04:47.113 looking up data that was available
NOTE Confidence: 0.919579350416667

00:04:47.113 --> 00:04:48.859 in the patients and then advising
NOTE Confidence: 0.919579350416667

00:04:48.859 --> 00:04:50.350 on clinical care of these patients
NOTE Confidence: 0.919579350416667

00:04:50.350 --> 00:04:52.341 and a lot of this was running by
NOTE Confidence: 0.919579350416667

00:04:52.341 --> 00:04:53.811 the seat of our pants because

NOTE Confidence: 0.919579350416667

00:04:53.811 --> 00:04:55.461 there wasn't a lot of data about

NOTE Confidence: 0.919579350416667

00:04:55.461 --> 00:04:56.706 how to manage these patients,

NOTE Confidence: 0.919579350416667

00:04:56.706 --> 00:04:59.233 but we were trying to sort of sift

NOTE Confidence: 0.919579350416667

00:04:59.233 --> 00:05:00.638 through the emerging case reports

NOTE Confidence: 0.919579350416667

00:05:00.638 --> 00:05:02.664 that were coming out while we were

NOTE Confidence: 0.919579350416667

00:05:02.664 --> 00:05:04.480 running this console service to try to.

NOTE Confidence: 0.919579350416667

00:05:04.480 --> 00:05:05.872 Harmonize what we were trying to

NOTE Confidence: 0.919579350416667

00:05:05.872 --> 00:05:07.350 do for these patients with what

NOTE Confidence: 0.919579350416667

00:05:07.350 --> 00:05:08.610 was happening around the world,

NOTE Confidence: 0.919579350416667

00:05:08.610 --> 00:05:10.296 and what other people have learned.

NOTE Confidence: 0.919579350416667

00:05:10.300 --> 00:05:12.228 And this is a snapshot of our sort

NOTE Confidence: 0.919579350416667

00:05:12.228 --> 00:05:14.524 of first 100 consoles that we saw on

NOTE Confidence: 0.919579350416667

00:05:14.524 --> 00:05:16.200 this neuro COVID console service,

NOTE Confidence: 0.919579350416667

00:05:16.200 --> 00:05:18.020 showing you the sort of panoply of

NOTE Confidence: 0.919579350416667

00:05:18.020 --> 00:05:19.716 different kinds of conditions of the

NOTE Confidence: 0.919579350416667

00:05:19.716 --> 00:05:21.542 consoles were forced so there was a
NOTE Confidence: 0.919579350416667

00:05:21.542 --> 00:05:23.110 large chunk of people who had had
NOTE Confidence: 0.919579350416667

00:05:23.165 --> 00:05:25.104 seizures in the setting of acute COVID.
NOTE Confidence: 0.919579350416667

00:05:25.110 --> 00:05:26.874 Most of these people were people who
NOTE Confidence: 0.919579350416667

00:05:26.874 --> 00:05:28.110 had underlying seizure disorders,
NOTE Confidence: 0.919579350416667

00:05:28.110 --> 00:05:29.974 and then they were coming in and in
NOTE Confidence: 0.919579350416667

00:05:29.974 --> 00:05:31.488 the setting of a febrile illness
NOTE Confidence: 0.790354097142857

00:05:31.490 --> 00:05:33.300 had a probably an unmasking
NOTE Confidence: 0.790354097142857

00:05:33.300 --> 00:05:34.882 of seizures, which is common.
NOTE Confidence: 0.790354097142857

00:05:34.882 --> 00:05:36.586 In anyone who has a seizure
NOTE Confidence: 0.790354097142857

00:05:36.586 --> 00:05:38.137 disorder when they have some
NOTE Confidence: 0.790354097142857

00:05:38.137 --> 00:05:39.652 other kind of systemic illness.
NOTE Confidence: 0.790354097142857

00:05:39.660 --> 00:05:42.240 But interestingly, 26% of these people
NOTE Confidence: 0.790354097142857

00:05:42.240 --> 00:05:44.660 had acute stroke during COVID-19,
NOTE Confidence: 0.790354097142857

00:05:44.660 --> 00:05:46.160 and then we had another large
NOTE Confidence: 0.790354097142857

00:05:46.160 --> 00:05:47.861 swath of people who would have

NOTE Confidence: 0.790354097142857
00:05:47.861 --> 00:05:49.466 what we called himself allopathy.
NOTE Confidence: 0.790354097142857
00:05:49.470 --> 00:05:51.808 And most of these people were either
NOTE Confidence: 0.790354097142857
00:05:51.808 --> 00:05:53.341 people who presented initially
NOTE Confidence: 0.790354097142857
00:05:53.341 --> 00:05:55.740 with confusion as as a primary
NOTE Confidence: 0.790354097142857
00:05:55.740 --> 00:05:57.200 presenting symptom of COVID,
NOTE Confidence: 0.790354097142857
00:05:57.200 --> 00:05:58.992 or there were people who had what
NOTE Confidence: 0.790354097142857
00:05:58.992 --> 00:06:01.239 we sort of thought in the end
NOTE Confidence: 0.790354097142857
00:06:01.239 --> 00:06:02.659 was encephalopathy or difficulty
NOTE Confidence: 0.790354097142857
00:06:02.659 --> 00:06:04.648 waking up out of proportion to,
NOTE Confidence: 0.790354097142857
00:06:04.650 --> 00:06:05.508 for example,
NOTE Confidence: 0.790354097142857
00:06:05.508 --> 00:06:07.653 situation or other aspects of
NOTE Confidence: 0.790354097142857
00:06:07.653 --> 00:06:08.940 their systemic illness.
NOTE Confidence: 0.790354097142857
00:06:08.940 --> 00:06:10.326 That's a difficult thing to term,
NOTE Confidence: 0.790354097142857
00:06:10.330 --> 00:06:12.045 because of course a lot of people
NOTE Confidence: 0.790354097142857
00:06:12.045 --> 00:06:13.385 have just hospital delirium in
NOTE Confidence: 0.790354097142857

00:06:13.385 --> 00:06:14.765 the setting of acute illness,
NOTE Confidence: 0.790354097142857

00:06:14.770 --> 00:06:16.198 but these were people that seem
NOTE Confidence: 0.790354097142857

00:06:16.198 --> 00:06:17.703 to really have more of this
NOTE Confidence: 0.790354097142857

00:06:17.703 --> 00:06:18.968 than would have been expected,
NOTE Confidence: 0.790354097142857

00:06:18.970 --> 00:06:20.770 and you can see there are also some other.
NOTE Confidence: 0.790354097142857

00:06:20.770 --> 00:06:21.530 Some conditions,
NOTE Confidence: 0.790354097142857

00:06:21.530 --> 00:06:23.050 including neuromuscular diseases and
NOTE Confidence: 0.790354097142857

00:06:23.050 --> 00:06:25.527 a few people who had acute psychosis
NOTE Confidence: 0.790354097142857

00:06:25.527 --> 00:06:27.620 in the sort of Perry COVID setting,
NOTE Confidence: 0.790354097142857

00:06:27.620 --> 00:06:29.456 which I'll talk about more later,
NOTE Confidence: 0.790354097142857

00:06:29.460 --> 00:06:31.188 and what we determined was that
NOTE Confidence: 0.790354097142857

00:06:31.188 --> 00:06:33.084 there were sort of two major
NOTE Confidence: 0.790354097142857

00:06:33.084 --> 00:06:35.118 categories of conditions that we saw.
NOTE Confidence: 0.790354097142857

00:06:35.120 --> 00:06:36.692 One were cerebral vascular
NOTE Confidence: 0.790354097142857

00:06:36.692 --> 00:06:38.657 injury or stroke and and,
NOTE Confidence: 0.790354097142857

00:06:38.660 --> 00:06:40.628 and this was something that was

NOTE Confidence: 0.790354097142857
00:06:40.630 --> 00:06:42.555 known to be potentially associated
NOTE Confidence: 0.790354097142857
00:06:42.555 --> 00:06:44.480 with clotting factors that are
NOTE Confidence: 0.790354097142857
00:06:44.543 --> 00:06:46.498 elevated in people with COVID-19,
NOTE Confidence: 0.790354097142857
00:06:46.500 --> 00:06:47.970 but also due to additional
NOTE Confidence: 0.790354097142857
00:06:47.970 --> 00:06:49.146 research investigation we did
NOTE Confidence: 0.790354097142857
00:06:49.146 --> 00:06:50.637 in some of these patients,
NOTE Confidence: 0.790354097142857
00:06:50.640 --> 00:06:51.680 we found that this also
NOTE Confidence: 0.790354097142857
00:06:51.680 --> 00:06:52.720 seemed to be associated with.
NOTE Confidence: 0.790354097142857
00:06:52.720 --> 00:06:54.944 Endothelial inflammation and activation
NOTE Confidence: 0.790354097142857
00:06:54.944 --> 00:06:58.573 in the setting of acute COVID-19 and
NOTE Confidence: 0.790354097142857
00:06:58.573 --> 00:07:00.917 the rest of the conditions that we saw.
NOTE Confidence: 0.790354097142857
00:07:00.920 --> 00:07:02.560 Although they were quite diverse,
NOTE Confidence: 0.790354097142857
00:07:02.560 --> 00:07:04.498 we ended up considering them to
NOTE Confidence: 0.790354097142857
00:07:04.498 --> 00:07:06.414 fall mostly in the categories
NOTE Confidence: 0.790354097142857
00:07:06.414 --> 00:07:08.614 of immune mediated neurologic
NOTE Confidence: 0.790354097142857

00:07:08.614 --> 00:07:10.264 and psychiatric conditions,
NOTE Confidence: 0.790354097142857

00:07:10.270 --> 00:07:12.139 and that was mostly based on the
NOTE Confidence: 0.790354097142857

00:07:12.139 --> 00:07:13.619 types of presentations we're seeing.
NOTE Confidence: 0.790354097142857

00:07:13.620 --> 00:07:14.900 Things like key on beret,
NOTE Confidence: 0.790354097142857

00:07:14.900 --> 00:07:17.905 things like what look like
NOTE Confidence: 0.790354097142857

00:07:17.905 --> 00:07:19.936 autoimmune myositis and the
NOTE Confidence: 0.790354097142857

00:07:19.936 --> 00:07:22.001 neurologic conditions seem to be
NOTE Confidence: 0.790354097142857

00:07:22.001 --> 00:07:23.730 associated potentially with immune.
NOTE Confidence: 0.790354097142857

00:07:23.730 --> 00:07:26.570 Some inflammation.
NOTE Confidence: 0.790354097142857

00:07:26.570 --> 00:07:28.187 This is a really nice example of
NOTE Confidence: 0.790354097142857

00:07:28.187 --> 00:07:29.559 such an immune mediated course
NOTE Confidence: 0.790354097142857

00:07:29.559 --> 00:07:31.129 or something that we decided
NOTE Confidence: 0.790354097142857

00:07:31.129 --> 00:07:32.570 was probably immune mediated,
NOTE Confidence: 0.790354097142857

00:07:32.570 --> 00:07:35.216 so this was a 70 year old woman who
NOTE Confidence: 0.790354097142857

00:07:35.216 --> 00:07:37.146 presented to you in March of 2020.
NOTE Confidence: 0.790354097142857

00:07:37.150 --> 00:07:38.722 This was before we were screening

NOTE Confidence: 0.790354097142857
00:07:38.722 --> 00:07:40.572 everyone for COVID when they came into
NOTE Confidence: 0.790354097142857
00:07:40.572 --> 00:07:42.222 the hospital and she actually presented
NOTE Confidence: 0.790354097142857
00:07:42.222 --> 00:07:43.950 with confusion and a witness seizure.
NOTE Confidence: 0.790354097142857
00:07:43.950 --> 00:07:46.218 And so she she actually didn't have
NOTE Confidence: 0.790354097142857
00:07:46.218 --> 00:07:48.632 fever cough and a positive news or
NOTE Confidence: 0.790354097142857
00:07:48.632 --> 00:07:50.690 fringilla swab for COVID until Ford
NOTE Confidence: 0.790354097142857
00:07:50.762 --> 00:07:52.987 four days into her hospitalization.
NOTE Confidence: 0.790354097142857
00:07:52.990 --> 00:07:54.862 So prior to that she had an MRI and
NOTE Confidence: 0.790354097142857
00:07:54.862 --> 00:07:56.938 the MRI images are shown on the right.
NOTE Confidence: 0.790354097142857
00:07:56.940 --> 00:07:58.816 This is obviously a fairly abnormal MRI,
NOTE Confidence: 0.790354097142857
00:07:58.820 --> 00:08:00.884 but I think these are really this is
NOTE Confidence: 0.790354097142857
00:08:00.884 --> 00:08:02.648 Shane's brain atrophy and she has a
NOTE Confidence: 0.790354097142857
00:08:02.648 --> 00:08:03.853 really chronic microvascular changes
NOTE Confidence: 0.790354097142857
00:08:03.853 --> 00:08:06.459 and she had a history of risk factors
NOTE Confidence: 0.790354097142857
00:08:06.459 --> 00:08:08.319 for significant microvascular disease,
NOTE Confidence: 0.790354097142857

00:08:08.320 --> 00:08:10.120 but her LP was completely
NOTE Confidence: 0.790354097142857

00:08:10.120 --> 00:08:11.920 benign and two white cells,
NOTE Confidence: 0.790354097142857

00:08:11.920 --> 00:08:14.345 normal protein of PCR's for
NOTE Confidence: 0.790354097142857

00:08:14.345 --> 00:08:16.285 viruses were not detected.
NOTE Confidence: 0.790354097142857

00:08:16.290 --> 00:08:18.378 Once we found out that she had acute COVID,
NOTE Confidence: 0.842571092142857

00:08:18.380 --> 00:08:21.068 we also were able to do research testing
NOTE Confidence: 0.842571092142857

00:08:21.068 --> 00:08:23.092 and looking for COVID in her CSS.
NOTE Confidence: 0.842571092142857

00:08:23.092 --> 00:08:25.270 SRS could be 2 in her CSF by PCR
NOTE Confidence: 0.842571092142857

00:08:25.342 --> 00:08:28.027 metagenomic sequencing and viral culture.
NOTE Confidence: 0.842571092142857

00:08:28.030 --> 00:08:30.137 And the virus did not was not
NOTE Confidence: 0.842571092142857

00:08:30.137 --> 00:08:32.109 detected by any of these means.
NOTE Confidence: 0.842571092142857

00:08:32.110 --> 00:08:34.427 However, when we used more sort of
NOTE Confidence: 0.842571092142857

00:08:34.427 --> 00:08:36.556 research testing to look at inflammatory
NOTE Confidence: 0.842571092142857

00:08:36.556 --> 00:08:39.048 cytokines in the CSF of this patient,
NOTE Confidence: 0.842571092142857

00:08:39.050 --> 00:08:41.605 what we found was that compared to
NOTE Confidence: 0.842571092142857

00:08:41.605 --> 00:08:43.894 pre pandemic control samples that we

NOTE Confidence: 0.842571092142857
00:08:43.894 --> 00:08:46.150 had that were age matched controls.
NOTE Confidence: 0.842571092142857
00:08:46.150 --> 00:08:48.080 This patient, whose CSF cytokines
NOTE Confidence: 0.842571092142857
00:08:48.080 --> 00:08:50.420 are shown in the orange bars,
NOTE Confidence: 0.842571092142857
00:08:50.420 --> 00:08:52.156 had evidence of neuroinflammation
NOTE Confidence: 0.842571092142857
00:08:52.156 --> 00:08:55.874 and in fact some of this seem to be
NOTE Confidence: 0.842571092142857
00:08:55.874 --> 00:08:58.282 similar to the the patterns of CSF.
NOTE Confidence: 0.842571092142857
00:08:58.290 --> 00:09:00.348 Cytokines are similar to the plasma.
NOTE Confidence: 0.842571092142857
00:09:00.350 --> 00:09:01.658 But a couple of these markers,
NOTE Confidence: 0.842571092142857
00:09:01.660 --> 00:09:03.430 and in particular MCP one,
NOTE Confidence: 0.842571092142857
00:09:03.430 --> 00:09:05.470 was quite elevated in the CSF
NOTE Confidence: 0.842571092142857
00:09:05.470 --> 00:09:06.490 and this patient,
NOTE Confidence: 0.842571092142857
00:09:06.490 --> 00:09:08.746 although it was not elevated in the plasma.
NOTE Confidence: 0.842571092142857
00:09:08.750 --> 00:09:10.676 So this was the first clue that we had
NOTE Confidence: 0.842571092142857
00:09:10.676 --> 00:09:12.820 that made the underlying some of these
NOTE Confidence: 0.842571092142857
00:09:12.820 --> 00:09:14.480 encephalopathies that we were seeing.
NOTE Confidence: 0.842571092142857

00:09:14.480 --> 00:09:14.921 Potentially,
NOTE Confidence: 0.842571092142857
00:09:14.921 --> 00:09:16.685 it wasn't necessarily viral
NOTE Confidence: 0.842571092142857
00:09:16.685 --> 00:09:18.890 encephalitis in the common sense,
NOTE Confidence: 0.842571092142857
00:09:18.890 --> 00:09:20.510 where you see viral replication
NOTE Confidence: 0.842571092142857
00:09:20.510 --> 00:09:21.806 in the nervous system,
NOTE Confidence: 0.842571092142857
00:09:21.810 --> 00:09:23.595 but instead this was some kind of
NOTE Confidence: 0.842571092142857
00:09:23.595 --> 00:09:24.960 an immune mediated phenomenon,
NOTE Confidence: 0.842571092142857
00:09:24.960 --> 00:09:27.081 despite the fact that she had no
NOTE Confidence: 0.842571092142857
00:09:27.081 --> 00:09:29.069 increase in her CSF white cells.
NOTE Confidence: 0.842571092142857
00:09:29.070 --> 00:09:31.005 And this is a sort of busy looking slide,
NOTE Confidence: 0.842571092142857
00:09:31.010 --> 00:09:32.552 but it's just a reminder for
NOTE Confidence: 0.842571092142857
00:09:32.552 --> 00:09:34.229 me to point out that many,
NOTE Confidence: 0.842571092142857
00:09:34.230 --> 00:09:36.590 many of the reports that have come out
NOTE Confidence: 0.842571092142857
00:09:36.590 --> 00:09:38.751 that have been case reports clinically
NOTE Confidence: 0.842571092142857
00:09:38.751 --> 00:09:41.056 described patients during acute COVID-19
NOTE Confidence: 0.842571092142857
00:09:41.056 --> 00:09:44.004 that have neurologic and then also I

NOTE Confidence: 0.842571092142857
00:09:44.004 --> 00:09:45.734 think psychiatric conditions that can
NOTE Confidence: 0.842571092142857
00:09:45.734 --> 00:09:48.249 best be attributed to immune pairing,
NOTE Confidence: 0.842571092142857
00:09:48.250 --> 00:09:51.988 infectious or autoimmune kinds of ideologies,
NOTE Confidence: 0.842571092142857
00:09:51.990 --> 00:09:54.170 so acute necrotizing encephalopathy,
NOTE Confidence: 0.842571092142857
00:09:54.170 --> 00:09:55.805 Guillain Barre syndrome,
NOTE Confidence: 0.842571092142857
00:09:55.810 --> 00:09:56.530 acute flossin,
NOTE Confidence: 0.842571092142857
00:09:56.530 --> 00:09:57.970 my leitis and many,
NOTE Confidence: 0.842571092142857
00:09:57.970 --> 00:09:59.626 many cases that we've seen of.
NOTE Confidence: 0.842571092142857
00:09:59.630 --> 00:10:02.936 I'm small fiber sensory neuropathy or
NOTE Confidence: 0.842571092142857
00:10:02.940 --> 00:10:05.232 neuropathy's have all been described in
NOTE Confidence: 0.842571092142857
00:10:05.232 --> 00:10:08.099 the sort of Perry acute COVID period,
NOTE Confidence: 0.842571092142857
00:10:08.100 --> 00:10:11.375 and many of these cases have
NOTE Confidence: 0.842571092142857
00:10:11.375 --> 00:10:12.860 had normal workups.
NOTE Confidence: 0.842571092142857
00:10:12.860 --> 00:10:15.830 No CSF pleocytosis normal protein levels,
NOTE Confidence: 0.842571092142857
00:10:15.830 --> 00:10:18.386 but the clinical phenomena are are
NOTE Confidence: 0.842571092142857

00:10:18.386 --> 00:10:21.616 really what we see typically in
NOTE Confidence: 0.842571092142857

00:10:21.616 --> 00:10:24.508 postinfectious immune mediated disorders.
NOTE Confidence: 0.842571092142857

00:10:24.510 --> 00:10:25.752 I also wanted to touch on
NOTE Confidence: 0.842571092142857

00:10:25.752 --> 00:10:26.580 the issue of stroke,
NOTE Confidence: 0.842571092142857

00:10:26.580 --> 00:10:28.372 which was another major category that we
NOTE Confidence: 0.842571092142857

00:10:28.372 --> 00:10:30.659 saw and in in our hospitalized patients.
NOTE Confidence: 0.842571092142857

00:10:30.660 --> 00:10:32.260 And this was actually very
NOTE Confidence: 0.842571092142857

00:10:32.260 --> 00:10:33.860 very early on the pandemic.
NOTE Confidence: 0.842571092142857

00:10:33.860 --> 00:10:36.352 There was a report that was super
NOTE Confidence: 0.842571092142857

00:10:36.352 --> 00:10:38.215 frightening of young people under age
NOTE Confidence: 0.842571092142857

00:10:38.215 --> 00:10:41.452 50 who had a few or no risk factors
NOTE Confidence: 0.842571092142857

00:10:41.452 --> 00:10:43.527 for stroke presenting with large
NOTE Confidence: 0.842571092142857

00:10:43.527 --> 00:10:46.084 vessel in a major strokes in the
NOTE Confidence: 0.842571092142857

00:10:46.084 --> 00:10:48.729 setting of acute COVID for some people
NOTE Confidence: 0.842571092142857

00:10:48.729 --> 00:10:50.844 stroke was actually there presenting
NOTE Confidence: 0.842571092142857

00:10:50.844 --> 00:10:53.350 syndrome or symptom to the hospital.

NOTE Confidence: 0.842571092142857
00:10:53.350 --> 00:10:54.505 And there was this sort
NOTE Confidence: 0.842571092142857
00:10:54.505 --> 00:10:55.429 of avalanche of concern.
NOTE Confidence: 0.842571092142857
00:10:55.430 --> 00:10:57.113 There was a lot of press about these cases,
NOTE Confidence: 0.842571092142857
00:10:57.120 --> 00:10:58.912 thinking that we were going to see lots
NOTE Confidence: 0.842571092142857
00:10:58.912 --> 00:11:00.669 and lots of strokes in young people,
NOTE Confidence: 0.842571092142857
00:11:00.670 --> 00:11:03.022 and there are reasons to think that
NOTE Confidence: 0.842571092142857
00:11:03.022 --> 00:11:04.944 people with COVID-19 are at increased
NOTE Confidence: 0.842571092142857
00:11:04.944 --> 00:11:07.585 risk of stroke and this has to do
NOTE Confidence: 0.842571092142857
00:11:07.585 --> 00:11:09.388 with coagulopathies thrombocytopenia.
NOTE Confidence: 0.842571092142857
00:11:09.390 --> 00:11:11.616 Elevation of D dimers and other
NOTE Confidence: 0.842571092142857
00:11:11.616 --> 00:11:13.684 blood measures that are clearly
NOTE Confidence: 0.842571092142857
00:11:13.684 --> 00:11:16.219 reflected in the prothrombotic state.
NOTE Confidence: 0.854677013809524
00:11:16.220 --> 00:11:18.758 And the fact that there are ACE 2 receptors
NOTE Confidence: 0.854677013809524
00:11:18.758 --> 00:11:20.931 which are the receptors that are necessary
NOTE Confidence: 0.854677013809524
00:11:20.931 --> 00:11:23.490 for the virus to entry on the surface
NOTE Confidence: 0.854677013809524

00:11:23.490 --> 00:11:25.140 of endothelial cells and pericytes,
NOTE Confidence: 0.854677013809524

00:11:25.140 --> 00:11:27.702 that line the the blood vessels and
NOTE Confidence: 0.854677013809524

00:11:27.702 --> 00:11:29.388 cells theoretically could be leading
NOTE Confidence: 0.854677013809524

00:11:29.388 --> 00:11:31.394 to vascular inflammation and changes.
NOTE Confidence: 0.854677013809524

00:11:31.394 --> 00:11:34.010 So this was a major concern
NOTE Confidence: 0.854677013809524

00:11:34.088 --> 00:11:35.918 based on this first paper.
NOTE Confidence: 0.854677013809524

00:11:35.920 --> 00:11:37.460 But I think that what was really
NOTE Confidence: 0.854677013809524

00:11:37.460 --> 00:11:38.660 interesting to learn and I think,
NOTE Confidence: 0.854677013809524

00:11:38.660 --> 00:11:41.420 was borne out by our studies as well,
NOTE Confidence: 0.854677013809524

00:11:41.420 --> 00:11:43.620 is that in fact,
NOTE Confidence: 0.854677013809524

00:11:43.620 --> 00:11:46.342 in the the most sort of comprehensive
NOTE Confidence: 0.854677013809524

00:11:46.342 --> 00:11:48.653 studies have suggested that stroke in young
NOTE Confidence: 0.854677013809524

00:11:48.653 --> 00:11:51.120 people is not a big feature of COVID-19.
NOTE Confidence: 0.854677013809524

00:11:51.120 --> 00:11:51.774 Thank goodness.
NOTE Confidence: 0.854677013809524

00:11:51.774 --> 00:11:52.101 However,
NOTE Confidence: 0.854677013809524

00:11:52.101 --> 00:11:54.063 there are increased rates of stroke

NOTE Confidence: 0.854677013809524
00:11:54.063 --> 00:11:56.576 in people living with people who have COVID,
NOTE Confidence: 0.854677013809524
00:11:56.580 --> 00:11:59.108 so some of the best data that has
NOTE Confidence: 0.854677013809524
00:11:59.108 --> 00:12:00.897 really characterized in their logic
NOTE Confidence: 0.854677013809524
00:12:00.897 --> 00:12:02.349 and psychiatric complications of
NOTE Confidence: 0.854677013809524
00:12:02.349 --> 00:12:04.620 cute COVID has come out of the UK.
NOTE Confidence: 0.854677013809524
00:12:04.620 --> 00:12:06.006 And it's really because of course.
NOTE Confidence: 0.854677013809524
00:12:06.010 --> 00:12:07.100 They are able to do,
NOTE Confidence: 0.854677013809524
00:12:07.100 --> 00:12:09.098 you know they have a unified
NOTE Confidence: 0.854677013809524
00:12:09.098 --> 00:12:11.694 healthcare system and also a very very
NOTE Confidence: 0.854677013809524
00:12:11.694 --> 00:12:13.294 connected healthcare system where
NOTE Confidence: 0.854677013809524
00:12:13.294 --> 00:12:15.348 hospital records are shared between
NOTE Confidence: 0.854677013809524
00:12:15.348 --> 00:12:17.333 all of their different institutions
NOTE Confidence: 0.854677013809524
00:12:17.333 --> 00:12:19.618 and data is collected in uniform
NOTE Confidence: 0.854677013809524
00:12:19.618 --> 00:12:21.106 ways across their institutions,
NOTE Confidence: 0.854677013809524
00:12:21.110 --> 00:12:22.685 and so they're able to collect data
NOTE Confidence: 0.854677013809524

00:12:22.685 --> 00:12:24.470 in a very far standardized way.
NOTE Confidence: 0.854677013809524

00:12:24.470 --> 00:12:26.166 And this was one of the first reports
NOTE Confidence: 0.854677013809524

00:12:26.166 --> 00:12:27.512 that came out of what's called
NOTE Confidence: 0.854677013809524

00:12:27.512 --> 00:12:29.000 the Coro Nerve study in the UK,
NOTE Confidence: 0.854677013809524

00:12:29.000 --> 00:12:30.815 where essentially they surveyed many
NOTE Confidence: 0.854677013809524

00:12:30.815 --> 00:12:33.742 many hospitals in the UK system for any
NOTE Confidence: 0.854677013809524

00:12:33.742 --> 00:12:36.199 reported cases of people who had neurologic.
NOTE Confidence: 0.854677013809524

00:12:36.200 --> 00:12:38.186 Diseases and they saw sort of
NOTE Confidence: 0.854677013809524

00:12:38.186 --> 00:12:40.140 similar cases that were reported.
NOTE Confidence: 0.854677013809524

00:12:40.140 --> 00:12:40.560 Of course,
NOTE Confidence: 0.854677013809524

00:12:40.560 --> 00:12:41.820 there's bias is what gets reported,
NOTE Confidence: 0.854677013809524

00:12:41.820 --> 00:12:43.120 what gets looked at,
NOTE Confidence: 0.854677013809524

00:12:43.120 --> 00:12:45.070 but they also saw many cerebrovascular
NOTE Confidence: 0.854677013809524

00:12:45.134 --> 00:12:47.304 events in many cases of altered mental
NOTE Confidence: 0.854677013809524

00:12:47.304 --> 00:12:49.050 status and what was interesting here
NOTE Confidence: 0.854677013809524

00:12:49.050 --> 00:12:51.385 is that when they looked at the age

NOTE Confidence: 0.854677013809524

00:12:51.385 --> 00:12:53.071 ranges of who was getting these

NOTE Confidence: 0.854677013809524

00:12:53.071 --> 00:12:54.740 conditions in this particular study,

NOTE Confidence: 0.854677013809524

00:12:54.740 --> 00:12:56.762 what they found was that although

NOTE Confidence: 0.854677013809524

00:12:56.762 --> 00:12:58.472 cerebral vascular disease shown in

NOTE Confidence: 0.854677013809524

00:12:58.472 --> 00:13:00.308 these blue columns was actually much

NOTE Confidence: 0.854677013809524

00:13:00.308 --> 00:13:02.102 more predominant in older ages and

NOTE Confidence: 0.854677013809524

00:13:02.102 --> 00:13:04.343 picked between ages of 71 and 80.

NOTE Confidence: 0.854677013809524

00:13:04.343 --> 00:13:06.248 What they term neuro psychiatric.

NOTE Confidence: 0.854677013809524

00:13:06.250 --> 00:13:08.746 That really included altered mental status,

NOTE Confidence: 0.854677013809524

00:13:08.750 --> 00:13:09.917 peripheral nerve disorders,

NOTE Confidence: 0.854677013809524

00:13:09.917 --> 00:13:12.640 and then some cases of things like

NOTE Confidence: 0.854677013809524

00:13:12.705 --> 00:13:14.461 psychosis were actually happening,

NOTE Confidence: 0.854677013809524

00:13:14.461 --> 00:13:16.446 sort of throughout the lifespan,

NOTE Confidence: 0.854677013809524

00:13:16.450 --> 00:13:17.302 and in fact,

NOTE Confidence: 0.854677013809524

00:13:17.302 --> 00:13:19.290 one might even say that they were

NOTE Confidence: 0.854677013809524

00:13:19.360 --> 00:13:21.618 more common in people ages 21 to 60.
NOTE Confidence: 0.854677013809524

00:13:21.618 --> 00:13:23.593 So I think this is the first clue
NOTE Confidence: 0.854677013809524

00:13:23.593 --> 00:13:25.613 that there obviously are different
NOTE Confidence: 0.854677013809524

00:13:25.613 --> 00:13:27.229 types of ideologies underlying.
NOTE Confidence: 0.854677013809524

00:13:27.230 --> 00:13:29.258 They may just super vascular complications,
NOTE Confidence: 0.854677013809524

00:13:29.260 --> 00:13:31.126 and some of these other complications.
NOTE Confidence: 0.854677013809524

00:13:31.130 --> 00:13:32.834 And it was also our first clue that
NOTE Confidence: 0.854677013809524

00:13:32.834 --> 00:13:34.590 some of these major complications of
NOTE Confidence: 0.854677013809524

00:13:34.590 --> 00:13:36.498 COVID-19 may not only be affecting.
NOTE Confidence: 0.854677013809524

00:13:36.500 --> 00:13:38.866 Elderly people who are at highest risk
NOTE Confidence: 0.854677013809524

00:13:38.866 --> 00:13:41.529 of death from COVID but actually are
NOTE Confidence: 0.854677013809524

00:13:41.529 --> 00:13:43.905 also affecting people at younger ages.
NOTE Confidence: 0.854677013809524

00:13:43.910 --> 00:13:45.410 This is another beautiful study
NOTE Confidence: 0.854677013809524

00:13:45.410 --> 00:13:47.300 from the UK Koro Nerve group,
NOTE Confidence: 0.854677013809524

00:13:47.300 --> 00:13:49.360 though this UK surveillance study.
NOTE Confidence: 0.854677013809524

00:13:49.360 --> 00:13:51.262 So this was a slightly larger

NOTE Confidence: 0.854677013809524

00:13:51.262 --> 00:13:52.530 population that they published

NOTE Confidence: 0.854677013809524

00:13:52.589 --> 00:13:54.239 later where they again looked at

NOTE Confidence: 0.854677013809524

00:13:54.239 --> 00:13:56.594 people who had been reported to have

NOTE Confidence: 0.854677013809524

00:13:56.594 --> 00:13:58.194 neurologic or psychiatric conditions

NOTE Confidence: 0.854677013809524

00:13:58.200 --> 00:14:00.930 around the time of acute COVID-19,

NOTE Confidence: 0.938186078333333

00:14:00.930 --> 00:14:02.580 and they did something very clever,

NOTE Confidence: 0.938186078333333

00:14:02.580 --> 00:14:04.988 which is they tried to look to see

NOTE Confidence: 0.938186078333333

00:14:04.988 --> 00:14:07.413 when the onset of these different

NOTE Confidence: 0.938186078333333

00:14:07.413 --> 00:14:10.060 conditions were with respect to onset

NOTE Confidence: 0.938186078333333

00:14:10.060 --> 00:14:12.360 of respiratory symptoms of COVID.

NOTE Confidence: 0.938186078333333

00:14:12.360 --> 00:14:14.424 So on the Y axis in this figure.

NOTE Confidence: 0.938186078333333

00:14:14.430 --> 00:14:16.684 The zero point would be the onset

NOTE Confidence: 0.938186078333333

00:14:16.684 --> 00:14:18.558 of respiratory symptoms and then the

NOTE Confidence: 0.938186078333333

00:14:18.558 --> 00:14:20.532 widest point on the violin plot would

NOTE Confidence: 0.938186078333333

00:14:20.597 --> 00:14:22.541 be the the main time that the onset

NOTE Confidence: 0.938186078333333

00:14:22.541 --> 00:14:24.404 of this particular condition had
NOTE Confidence: 0.9381860783333333

00:14:24.404 --> 00:14:26.694 risen in these different patients,
NOTE Confidence: 0.9381860783333333

00:14:26.700 --> 00:14:28.653 and I think what this does is it gives
NOTE Confidence: 0.9381860783333333

00:14:28.653 --> 00:14:31.603 us a little bit of insight into again
NOTE Confidence: 0.9381860783333333

00:14:31.603 --> 00:14:32.749 potentially diverse pathophysiologies
NOTE Confidence: 0.9381860783333333

00:14:32.750 --> 00:14:35.030 of these different types of conditions,
NOTE Confidence: 0.9381860783333333

00:14:35.030 --> 00:14:37.670 and So what they found was that in
NOTE Confidence: 0.9381860783333333

00:14:37.670 --> 00:14:39.482 29% of people there were actually
NOTE Confidence: 0.9381860783333333

00:14:39.482 --> 00:14:41.707 neuro or sex symptoms that predated
NOTE Confidence: 0.9381860783333333

00:14:41.707 --> 00:14:42.667 respiratory symptoms.
NOTE Confidence: 0.9381860783333333

00:14:42.670 --> 00:14:43.937 And when you look at the figure,
NOTE Confidence: 0.9381860783333333

00:14:43.940 --> 00:14:45.825 it actually is primarily this
NOTE Confidence: 0.9381860783333333

00:14:45.825 --> 00:14:46.956 river vascular complications.
NOTE Confidence: 0.9381860783333333

00:14:46.960 --> 00:14:51.069 Starting very early and then our preceding
NOTE Confidence: 0.9381860783333333

00:14:51.069 --> 00:14:53.028 the relative respiratory symptoms.
NOTE Confidence: 0.9381860783333333

00:14:53.028 --> 00:14:55.764 Then there were another group of

NOTE Confidence: 0.938186078333333

00:14:55.770 --> 00:14:58.236 symptoms that were actually seen after

NOTE Confidence: 0.938186078333333

00:14:58.236 --> 00:14:59.880 the initial respiratory conditions.

NOTE Confidence: 0.938186078333333

00:14:59.880 --> 00:15:01.389 Severe respiratory system

NOTE Confidence: 0.938186078333333

00:15:01.389 --> 00:15:02.898 condition improved again.

NOTE Confidence: 0.938186078333333

00:15:02.900 --> 00:15:03.952 These were hospitalized patients,

NOTE Confidence: 0.938186078333333

00:15:03.952 --> 00:15:05.821 so many of these people were coming

NOTE Confidence: 0.938186078333333

00:15:05.821 --> 00:15:07.056 in with shortness of breath.

NOTE Confidence: 0.938186078333333

00:15:07.060 --> 00:15:09.040 Oxygen needs that kind of thing,

NOTE Confidence: 0.938186078333333

00:15:09.040 --> 00:15:12.211 but a good proportion of people actually

NOTE Confidence: 0.938186078333333

00:15:12.211 --> 00:15:15.341 develop their symptoms up to two weeks

NOTE Confidence: 0.938186078333333

00:15:15.341 --> 00:15:17.885 after the respiratory symptoms had started.

NOTE Confidence: 0.938186078333333

00:15:17.890 --> 00:15:19.122 And this was interesting,

NOTE Confidence: 0.938186078333333

00:15:19.122 --> 00:15:21.910 because these seem to be in what they

NOTE Confidence: 0.938186078333333

00:15:21.910 --> 00:15:24.115 termed central inflammatory psychiatric and

NOTE Confidence: 0.938186078333333

00:15:24.115 --> 00:15:26.490 peripheral nerve types of complications.

NOTE Confidence: 0.938186078333333

00:15:26.490 --> 00:15:27.170 And again this is,
NOTE Confidence: 0.9381860783333333

00:15:27.170 --> 00:15:27.510 I think,
NOTE Confidence: 0.9381860783333333

00:15:27.510 --> 00:15:29.406 reflective of what we've seen clinically,
NOTE Confidence: 0.9381860783333333

00:15:29.410 --> 00:15:32.042 and it suggests again that these are
NOTE Confidence: 0.9381860783333333

00:15:32.042 --> 00:15:34.405 likely immune mediated phenomena that are
NOTE Confidence: 0.9381860783333333

00:15:34.405 --> 00:15:37.128 somehow a response to the viral infection,
NOTE Confidence: 0.9381860783333333

00:15:37.130 --> 00:15:39.834 but maybe not directly caused by the virus.
NOTE Confidence: 0.9381860783333333

00:15:39.840 --> 00:15:40.348 So again,
NOTE Confidence: 0.9381860783333333

00:15:40.348 --> 00:15:42.806 this is another clue to kind of help us
NOTE Confidence: 0.9381860783333333

00:15:42.806 --> 00:15:44.984 understand the etiology of these disorders.
NOTE Confidence: 0.9381860783333333

00:15:44.990 --> 00:15:46.796 But what I've been telling you were
NOTE Confidence: 0.9381860783333333

00:15:46.796 --> 00:15:47.930 basically all clinical reports
NOTE Confidence: 0.9381860783333333

00:15:47.930 --> 00:15:49.378 and this has to do with the fact
NOTE Confidence: 0.9381860783333333

00:15:49.378 --> 00:15:50.529 that clinical data was collected.
NOTE Confidence: 0.9381860783333333

00:15:50.530 --> 00:15:51.128 Of course,
NOTE Confidence: 0.9381860783333333

00:15:51.128 --> 00:15:53.221 in all of these patients who were

NOTE Confidence: 0.938186078333333
00:15:53.221 --> 00:15:54.514 hospitalized but there weren't
NOTE Confidence: 0.938186078333333
00:15:54.514 --> 00:15:56.082 really systematic research studies
NOTE Confidence: 0.938186078333333
00:15:56.082 --> 00:15:57.650 done at that time.
NOTE Confidence: 0.938186078333333
00:15:57.650 --> 00:15:59.970 And what we have learned,
NOTE Confidence: 0.938186078333333
00:15:59.970 --> 00:16:00.334 though,
NOTE Confidence: 0.938186078333333
00:16:00.334 --> 00:16:02.882 are that even small numbers of of
NOTE Confidence: 0.938186078333333
00:16:02.882 --> 00:16:04.641 systematic research can be helpful
NOTE Confidence: 0.938186078333333
00:16:04.641 --> 00:16:06.246 in trying to understand HIV.
NOTE Confidence: 0.938186078333333
00:16:06.250 --> 00:16:09.466 I'm sorry, acute COVID-19 era pathogenesis,
NOTE Confidence: 0.938186078333333
00:16:09.470 --> 00:16:11.726 and I just wanted to do a really
NOTE Confidence: 0.938186078333333
00:16:11.726 --> 00:16:13.168 quick review of the virus.
NOTE Confidence: 0.938186078333333
00:16:13.170 --> 00:16:14.955 For those of you who are not
NOTE Confidence: 0.938186078333333
00:16:14.955 --> 00:16:15.465 completely tired.
NOTE Confidence: 0.938186078333333
00:16:15.470 --> 00:16:16.526 Is remembering exactly what
NOTE Confidence: 0.938186078333333
00:16:16.526 --> 00:16:17.846 the structure is of cart.
NOTE Confidence: 0.938186078333333

00:16:17.850 --> 00:16:19.674 Stars could be 2 and what the viral
NOTE Confidence: 0.9381860783333333

00:16:19.674 --> 00:16:21.320 life cycle is probably most of us
NOTE Confidence: 0.9381860783333333

00:16:21.320 --> 00:16:23.252 know this way more than we would ever
NOTE Confidence: 0.9381860783333333

00:16:23.252 --> 00:16:24.981 want to know anything about a virus,
NOTE Confidence: 0.9381860783333333

00:16:24.990 --> 00:16:28.000 but just as a reminder.
NOTE Confidence: 0.9381860783333333

00:16:28.000 --> 00:16:29.220 We've known since very,
NOTE Confidence: 0.9381860783333333

00:16:29.220 --> 00:16:31.613 very early in the pandemic that this is
NOTE Confidence: 0.9381860783333333

00:16:31.613 --> 00:16:34.060 a very simple virus with a single RNA strand.
NOTE Confidence: 0.9381860783333333

00:16:34.060 --> 00:16:34.584 Very,
NOTE Confidence: 0.9381860783333333

00:16:34.584 --> 00:16:38.020 very few proteins encoded and the
NOTE Confidence: 0.9381860783333333

00:16:38.020 --> 00:16:41.370 virus is surrounded by a.
NOTE Confidence: 0.9381860783333333

00:16:41.370 --> 00:16:43.800 Declare capsid and then a.
NOTE Confidence: 0.9381860783333333

00:16:43.800 --> 00:16:45.678 Sorry it's bye bye and envelope
NOTE Confidence: 0.9381860783333333

00:16:45.678 --> 00:16:47.596 proteins and then there are spike
NOTE Confidence: 0.9381860783333333

00:16:47.596 --> 00:16:49.408 trimers that emerge from the surface
NOTE Confidence: 0.9381860783333333

00:16:49.408 --> 00:16:51.277 of the virus and these spike

NOTE Confidence: 0.938186078333333

00:16:51.277 --> 00:16:53.089 trimers are again what the most

NOTE Confidence: 0.835962504285714

00:16:53.090 --> 00:16:56.240 of our RNA antibodies are directed against.

NOTE Confidence: 0.835962504285714

00:16:56.240 --> 00:16:57.800 I'm sorry vaccinations are

NOTE Confidence: 0.835962504285714

00:16:57.800 --> 00:16:58.970 directed against these.

NOTE Confidence: 0.835962504285714

00:16:58.970 --> 00:17:02.039 Spike trimers are.

NOTE Confidence: 0.835962504285714

00:17:02.040 --> 00:17:03.408 Basically, what's needed to

NOTE Confidence: 0.835962504285714

00:17:03.408 --> 00:17:05.460 be recognized by a host cell,

NOTE Confidence: 0.835962504285714

00:17:05.460 --> 00:17:07.748 so the ACE 2 receptor on the surface

NOTE Confidence: 0.835962504285714

00:17:07.748 --> 00:17:09.615 of mammalian cells is recognized as

NOTE Confidence: 0.835962504285714

00:17:09.615 --> 00:17:12.056 the spike trimmer of the virus and it

NOTE Confidence: 0.835962504285714

00:17:12.056 --> 00:17:14.152 allows for entry of virus into a cell.

NOTE Confidence: 0.835962504285714

00:17:14.160 --> 00:17:16.715 So the presence of ACE 2 receptors

NOTE Confidence: 0.835962504285714

00:17:16.715 --> 00:17:19.318 and then other related receptors and

NOTE Confidence: 0.835962504285714

00:17:19.318 --> 00:17:22.060 other proteins that allow for binding

NOTE Confidence: 0.835962504285714

00:17:22.060 --> 00:17:24.883 and entry of the virus is really what

NOTE Confidence: 0.835962504285714

00:17:24.883 --> 00:17:26.929 determines the cellular tropism of this
NOTE Confidence: 0.835962504285714

00:17:26.929 --> 00:17:28.929 virus and determines what types of
NOTE Confidence: 0.835962504285714

00:17:28.929 --> 00:17:31.150 cells and tissues the virus can enter.
NOTE Confidence: 0.835962504285714

00:17:31.150 --> 00:17:32.152 And then I also wanted to
NOTE Confidence: 0.835962504285714

00:17:32.152 --> 00:17:33.410 remind you with a figure on the.
NOTE Confidence: 0.835962504285714

00:17:33.410 --> 00:17:35.723 Right, but the viral life cycle is for SARS,
NOTE Confidence: 0.835962504285714

00:17:35.730 --> 00:17:38.930 Co V2 and essentially this is an RNA
NOTE Confidence: 0.835962504285714

00:17:38.930 --> 00:17:41.425 virus that uses the host cytoplasmic
NOTE Confidence: 0.835962504285714

00:17:41.425 --> 00:17:43.900 cell machinery to replicate itself.
NOTE Confidence: 0.835962504285714

00:17:43.900 --> 00:17:45.523 So unlike HIV,
NOTE Confidence: 0.835962504285714

00:17:45.523 --> 00:17:48.332 another RNA virus which actually uses
NOTE Confidence: 0.835962504285714

00:17:48.332 --> 00:17:49.908 reverse transcriptase to integrate
NOTE Confidence: 0.835962504285714

00:17:49.908 --> 00:17:52.049 its genome into our host genome,
NOTE Confidence: 0.835962504285714

00:17:52.050 --> 00:17:54.290 which is why this is a chronic and
NOTE Confidence: 0.835962504285714

00:17:54.290 --> 00:17:55.310 essentially incurable disease,
NOTE Confidence: 0.835962504285714

00:17:55.310 --> 00:17:57.361 except for three people out of 75

NOTE Confidence: 0.835962504285714

00:17:57.361 --> 00:17:59.770 million people have had it in SARS, Co.

NOTE Confidence: 0.835962504285714

00:17:59.770 --> 00:18:00.150 V2.

NOTE Confidence: 0.835962504285714

00:18:00.150 --> 00:18:02.430 The virus does not become hopefully

NOTE Confidence: 0.835962504285714

00:18:02.512 --> 00:18:04.267 as far as we understand.

NOTE Confidence: 0.835962504285714

00:18:04.270 --> 00:18:04.910 Chronic illness.

NOTE Confidence: 0.835962504285714

00:18:04.910 --> 00:18:07.150 It's an acute illness that uses the

NOTE Confidence: 0.835962504285714

00:18:07.150 --> 00:18:09.387 host machinery to make more of itself.

NOTE Confidence: 0.835962504285714

00:18:09.390 --> 00:18:11.675 But eventually, when the immune

NOTE Confidence: 0.835962504285714

00:18:11.675 --> 00:18:14.066 system can kill the infected cells,

NOTE Confidence: 0.835962504285714

00:18:14.066 --> 00:18:16.280 then the virus will die out.

NOTE Confidence: 0.835962504285714

00:18:16.280 --> 00:18:18.368 So what do we know about how this

NOTE Confidence: 0.835962504285714

00:18:18.368 --> 00:18:20.459 virus might affect the nervous system?

NOTE Confidence: 0.835962504285714

00:18:20.460 --> 00:18:22.516 And some of it is indicated by some

NOTE Confidence: 0.835962504285714

00:18:22.516 --> 00:18:24.853 of it initially was indicated by what

NOTE Confidence: 0.835962504285714

00:18:24.853 --> 00:18:27.180 we knew by prior similar viruses.

NOTE Confidence: 0.835962504285714

00:18:27.180 --> 00:18:28.006 So SARS,
NOTE Confidence: 0.835962504285714

00:18:28.006 --> 00:18:30.897 Co V2 has a lot of nucleotide
NOTE Confidence: 0.835962504285714

00:18:30.897 --> 00:18:33.430 identity to prior coronaviruses.
NOTE Confidence: 0.835962504285714

00:18:33.430 --> 00:18:34.558 In particular SARS,
NOTE Confidence: 0.835962504285714

00:18:34.558 --> 00:18:36.814 Co V1 and the mayor's virus.
NOTE Confidence: 0.835962504285714

00:18:36.820 --> 00:18:38.780 This is important because there
NOTE Confidence: 0.835962504285714

00:18:38.780 --> 00:18:40.348 were actually known neurologic
NOTE Confidence: 0.835962504285714

00:18:40.348 --> 00:18:41.680 complications even though very,
NOTE Confidence: 0.835962504285714

00:18:41.680 --> 00:18:43.610 very few people worldwide contracted
NOTE Confidence: 0.835962504285714

00:18:43.610 --> 00:18:45.154 either of those infections.
NOTE Confidence: 0.835962504285714

00:18:45.160 --> 00:18:47.029 But some of what we knew originally
NOTE Confidence: 0.835962504285714

00:18:47.029 --> 00:18:47.563 about how.
NOTE Confidence: 0.835962504285714

00:18:47.570 --> 00:18:49.375 Starts Kaviti might affect the
NOTE Confidence: 0.835962504285714

00:18:49.375 --> 00:18:51.180 nervous system was learned from
NOTE Confidence: 0.835962504285714

00:18:51.246 --> 00:18:53.126 these earlier outbreaks and what
NOTE Confidence: 0.835962504285714

00:18:53.126 --> 00:18:54.630 was understood from them.

NOTE Confidence: 0.835962504285714

00:18:54.630 --> 00:18:56.807 And one of the early concerns was

NOTE Confidence: 0.835962504285714

00:18:56.807 --> 00:18:59.361 whether or not stars could be 2 might

NOTE Confidence: 0.835962504285714

00:18:59.361 --> 00:19:01.630 enter and infect cells in the brain.

NOTE Confidence: 0.835962504285714

00:19:01.630 --> 00:19:03.583 So why would we think that could be possible?

NOTE Confidence: 0.835962504285714

00:19:03.590 --> 00:19:03.859 Well,

NOTE Confidence: 0.835962504285714

00:19:03.859 --> 00:19:05.473 one thing that's known is that

NOTE Confidence: 0.835962504285714

00:19:05.473 --> 00:19:06.970 stars that ACE 2 receptors,

NOTE Confidence: 0.835962504285714

00:19:06.970 --> 00:19:07.442 which again,

NOTE Confidence: 0.835962504285714

00:19:07.442 --> 00:19:08.150 as I mentioned,

NOTE Confidence: 0.835962504285714

00:19:08.150 --> 00:19:10.411 allow for entry of virus into cells

NOTE Confidence: 0.835962504285714

00:19:10.411 --> 00:19:12.483 and into tissues are actually located

NOTE Confidence: 0.835962504285714

00:19:12.483 --> 00:19:14.912 on multiple cell types in the body,

NOTE Confidence: 0.835962504285714

00:19:14.920 --> 00:19:17.164 and although there are very very

NOTE Confidence: 0.835962504285714

00:19:17.164 --> 00:19:19.781 common in the nasopharynx and in the

NOTE Confidence: 0.835962504285714

00:19:19.781 --> 00:19:21.887 alveolar epithelial cells of the lung,

NOTE Confidence: 0.835962504285714

00:19:21.890 --> 00:19:24.404 probably explaining why most of those
NOTE Confidence: 0.835962504285714

00:19:24.404 --> 00:19:27.149 are these major major target organs,
NOTE Confidence: 0.835962504285714

00:19:27.150 --> 00:19:29.446 other target organs also include the kidney,
NOTE Confidence: 0.835962504285714

00:19:29.450 --> 00:19:31.210 the intestines, the blood vessels,
NOTE Confidence: 0.835962504285714

00:19:31.210 --> 00:19:32.998 and the nervous system.
NOTE Confidence: 0.835962504285714

00:19:32.998 --> 00:19:35.380 And as again, we all learn very,
NOTE Confidence: 0.835962504285714

00:19:35.380 --> 00:19:36.680 very quickly in the first
NOTE Confidence: 0.835962504285714

00:19:36.680 --> 00:19:37.810 months of the pandemic,
NOTE Confidence: 0.835962504285714

00:19:37.810 --> 00:19:40.001 all of these organs can actually be
NOTE Confidence: 0.835962504285714

00:19:40.001 --> 00:19:42.158 affected in people with acute COVID-19.
NOTE Confidence: 0.835962504285714

00:19:42.160 --> 00:19:43.860 And what we didn't know,
NOTE Confidence: 0.835962504285714

00:19:43.860 --> 00:19:44.323 however,
NOTE Confidence: 0.835962504285714

00:19:44.323 --> 00:19:46.175 is which actual cells
NOTE Confidence: 0.835962504285714

00:19:46.175 --> 00:19:48.490 of the brain express ACE
NOTE Confidence: 0.794358251166667

00:19:48.574 --> 00:19:51.532 2 receptors and on the right you can see a
NOTE Confidence: 0.794358251166667

00:19:51.532 --> 00:19:54.585 very nice in silico analysis looking for the

NOTE Confidence: 0.794358251166667

00:19:54.585 --> 00:19:56.940 distribution of genes relevant to severe.

NOTE Confidence: 0.794358251166667

00:19:56.940 --> 00:20:00.846 So stars Kobe 2IN different cell types in the

NOTE Confidence: 0.794358251166667

00:20:00.846 --> 00:20:03.143 brain and what you can see is that ACE 2.

NOTE Confidence: 0.794358251166667

00:20:03.150 --> 00:20:05.780 Actually seems to have only

NOTE Confidence: 0.794358251166667

00:20:05.780 --> 00:20:07.884 modest expression in neurons.

NOTE Confidence: 0.794358251166667

00:20:07.890 --> 00:20:10.014 It does seem to have higher

NOTE Confidence: 0.794358251166667

00:20:10.014 --> 00:20:11.076 expression in oligodendrocytes,

NOTE Confidence: 0.794358251166667

00:20:11.080 --> 00:20:13.488 but some of these other proteins that

NOTE Confidence: 0.794358251166667

00:20:13.488 --> 00:20:15.696 are important for viral entry are

NOTE Confidence: 0.794358251166667

00:20:15.696 --> 00:20:17.910 also are highly expressed in neurons,

NOTE Confidence: 0.794358251166667

00:20:17.910 --> 00:20:19.884 suggesting that there may be some

NOTE Confidence: 0.794358251166667

00:20:19.884 --> 00:20:23.390 vulnerability of neurons to SARS, Co V2,

NOTE Confidence: 0.794358251166667

00:20:23.390 --> 00:20:25.707 but but we don't have strong expression

NOTE Confidence: 0.794358251166667

00:20:25.707 --> 00:20:28.569 of ACE 2 on the surface of neurons.

NOTE Confidence: 0.794358251166667

00:20:28.570 --> 00:20:29.767 How would the virus get to the

NOTE Confidence: 0.794358251166667

00:20:29.767 --> 00:20:30.720 brain in the 1st place?
NOTE Confidence: 0.794358251166667

00:20:30.720 --> 00:20:32.460 I think this is again something
NOTE Confidence: 0.794358251166667

00:20:32.460 --> 00:20:34.631 that that many of the positive sort
NOTE Confidence: 0.794358251166667

00:20:34.631 --> 00:20:36.515 of mechanisms were based on what
NOTE Confidence: 0.794358251166667

00:20:36.515 --> 00:20:38.319 we knew from prior viruses.
NOTE Confidence: 0.794358251166667

00:20:38.320 --> 00:20:40.444 So this is a model that we put together
NOTE Confidence: 0.794358251166667

00:20:40.444 --> 00:20:42.300 back again in March or April 2020,
NOTE Confidence: 0.794358251166667

00:20:42.300 --> 00:20:42.942 saying well,
NOTE Confidence: 0.794358251166667

00:20:42.942 --> 00:20:44.868 one possibility is the virus could
NOTE Confidence: 0.794358251166667

00:20:44.868 --> 00:20:46.706 potentially get into the brain by
NOTE Confidence: 0.794358251166667

00:20:46.706 --> 00:20:48.131 haematogenous spread and this model
NOTE Confidence: 0.794358251166667

00:20:48.131 --> 00:20:49.825 is based essentially on the model
NOTE Confidence: 0.794358251166667

00:20:49.825 --> 00:20:51.830 that we know for other viruses,
NOTE Confidence: 0.794358251166667

00:20:51.830 --> 00:20:55.730 including HIV where viral particles but
NOTE Confidence: 0.794358251166667

00:20:55.730 --> 00:20:59.049 particularly infect virally infected cells.
NOTE Confidence: 0.794358251166667

00:20:59.050 --> 00:21:01.408 May traffic through the vascular endothelium

NOTE Confidence: 0.794358251166667

00:21:01.408 --> 00:21:04.488 in the blood brain barrier into the brain?

NOTE Confidence: 0.794358251166667

00:21:04.490 --> 00:21:06.620 I think that this is something

NOTE Confidence: 0.794358251166667

00:21:06.620 --> 00:21:08.880 that was a potential hypothesis.

NOTE Confidence: 0.794358251166667

00:21:08.880 --> 00:21:12.910 It turns out that SARS Co V2 is not really

NOTE Confidence: 0.794358251166667

00:21:12.910 --> 00:21:14.794 readily detectable in the blood and

NOTE Confidence: 0.794358251166667

00:21:14.794 --> 00:21:17.488 many people who are very sick with COVID-19.

NOTE Confidence: 0.794358251166667

00:21:17.490 --> 00:21:20.258 So in fact it's there's not as much

NOTE Confidence: 0.794358251166667

00:21:20.258 --> 00:21:23.042 SARS Co V2 viraemia as there is

NOTE Confidence: 0.794358251166667

00:21:23.042 --> 00:21:24.585 for example collection of stars.

NOTE Confidence: 0.794358251166667

00:21:24.585 --> 00:21:26.055 Kobe 2 virus and things like

NOTE Confidence: 0.794358251166667

00:21:26.055 --> 00:21:27.510 the whole factory epithelium,

NOTE Confidence: 0.794358251166667

00:21:27.510 --> 00:21:29.160 which makes I think this.

NOTE Confidence: 0.794358251166667

00:21:29.160 --> 00:21:31.148 Hematogenous spread a little bit less likely,

NOTE Confidence: 0.794358251166667

00:21:31.150 --> 00:21:32.950 although still a potential in,

NOTE Confidence: 0.794358251166667

00:21:32.950 --> 00:21:34.810 especially maybe in people with a

NOTE Confidence: 0.794358251166667

00:21:34.810 --> 00:21:37.184 breakdown of the blood brain barrier on
NOTE Confidence: 0.794358251166667

00:21:37.184 --> 00:21:39.308 the right is another transcranial root,
NOTE Confidence: 0.794358251166667

00:21:39.310 --> 00:21:41.926 which I think is potentially sort
NOTE Confidence: 0.794358251166667

00:21:41.926 --> 00:21:44.432 of more likely if there really is
NOTE Confidence: 0.794358251166667

00:21:44.432 --> 00:21:46.220 viral entry into the brain that
NOTE Confidence: 0.794358251166667

00:21:46.281 --> 00:21:48.006 it could be entering through.
NOTE Confidence: 0.794358251166667

00:21:48.010 --> 00:21:50.044 There's robust infection of the system
NOTE Confidence: 0.794358251166667

00:21:50.044 --> 00:21:52.135 tacular cells and the whole factory
NOTE Confidence: 0.794358251166667

00:21:52.135 --> 00:21:54.169 epithelium in the news of pharynx.
NOTE Confidence: 0.794358251166667

00:21:54.170 --> 00:21:56.543 This may be related to the anosmia
NOTE Confidence: 0.794358251166667

00:21:56.543 --> 00:21:59.254 that probably at least half of people
NOTE Confidence: 0.794358251166667

00:21:59.254 --> 00:22:01.284 experience when they get COVID-19.
NOTE Confidence: 0.794358251166667

00:22:01.290 --> 00:22:03.740 And the sub position was is the
NOTE Confidence: 0.794358251166667

00:22:03.740 --> 00:22:05.266 potentially the olfactory nerves
NOTE Confidence: 0.794358251166667

00:22:05.266 --> 00:22:07.301 could then locally become infected
NOTE Confidence: 0.794358251166667

00:22:07.301 --> 00:22:09.350 and through retrograde spread

NOTE Confidence: 0.794358251166667
00:22:09.350 --> 00:22:12.425 through between the synaptic cleft.
NOTE Confidence: 0.794358251166667
00:22:12.430 --> 00:22:14.698 The virus could then be transmitted into
NOTE Confidence: 0.794358251166667
00:22:14.698 --> 00:22:16.778 the olfactory bulb and into the brain.
NOTE Confidence: 0.794358251166667
00:22:16.780 --> 00:22:19.348 This has been shown to be possible by
NOTE Confidence: 0.794358251166667
00:22:19.348 --> 00:22:21.419 concerns COVIE 1 using animal models,
NOTE Confidence: 0.794358251166667
00:22:21.420 --> 00:22:23.916 and so this was really a putative mechanism.
NOTE Confidence: 0.794358251166667
00:22:23.920 --> 00:22:25.495 But what's the evidence that stars could
NOTE Confidence: 0.794358251166667
00:22:25.495 --> 00:22:27.520 be to you actually gets into the brain?
NOTE Confidence: 0.794358251166667
00:22:27.520 --> 00:22:29.386 I think there's really not a
NOTE Confidence: 0.794358251166667
00:22:29.386 --> 00:22:30.630 lot of evidence so.
NOTE Confidence: 0.794358251166667
00:22:30.630 --> 00:22:32.694 There have been a number of studies that
NOTE Confidence: 0.794358251166667
00:22:32.694 --> 00:22:35.069 have used small samples of looking for stars.
NOTE Confidence: 0.794358251166667
00:22:35.070 --> 00:22:37.350 Kobe 2 for example in CSF fluid and
NOTE Confidence: 0.794358251166667
00:22:37.350 --> 00:22:39.624 all of you know that super spinal
NOTE Confidence: 0.794358251166667
00:22:39.624 --> 00:22:41.254 fluid is not the same
NOTE Confidence: 0.828827753913044

00:22:41.326 --> 00:22:43.355 as the brain. It's not telling us about
NOTE Confidence: 0.828827753913044

00:22:43.355 --> 00:22:44.909 what's happening in the deep brain
NOTE Confidence: 0.828827753913044

00:22:44.909 --> 00:22:47.205 parenchyma, but in many many acute
NOTE Confidence: 0.828827753913044

00:22:47.205 --> 00:22:49.573 viral infections of viral particles are
NOTE Confidence: 0.828827753913044

00:22:49.573 --> 00:22:51.775 readily detected in the spinal fluid
NOTE Confidence: 0.828827753913044

00:22:51.775 --> 00:22:54.208 in the setting of brain infection,
NOTE Confidence: 0.828827753913044

00:22:54.210 --> 00:22:56.070 acute HIV being something I've been
NOTE Confidence: 0.828827753913044

00:22:56.070 --> 00:22:58.349 studying for 20 years is a good example.
NOTE Confidence: 0.828827753913044

00:22:58.350 --> 00:23:01.090 We're about 80 or 90% of people during acute.
NOTE Confidence: 0.828827753913044

00:23:01.090 --> 00:23:01.810 Striking infection,
NOTE Confidence: 0.828827753913044

00:23:01.810 --> 00:23:03.502 even without any symptoms,
NOTE Confidence: 0.828827753913044

00:23:03.502 --> 00:23:05.194 have readily detectable HIV
NOTE Confidence: 0.828827753913044

00:23:05.194 --> 00:23:07.290 RNA in the spinal fluid.
NOTE Confidence: 0.828827753913044

00:23:07.290 --> 00:23:08.518 But interestingly,
NOTE Confidence: 0.828827753913044

00:23:08.518 --> 00:23:11.588 in people with acute COVID-19,
NOTE Confidence: 0.828827753913044

00:23:11.590 --> 00:23:13.130 particularly looking at people

NOTE Confidence: 0.828827753913044
00:23:13.130 --> 00:23:14.285 with neurologic symptoms,
NOTE Confidence: 0.828827753913044
00:23:14.290 --> 00:23:15.662 there have been very,
NOTE Confidence: 0.828827753913044
00:23:15.662 --> 00:23:17.377 very little a few reports
NOTE Confidence: 0.828827753913044
00:23:17.377 --> 00:23:19.268 suggesting that one can detect SARS.
NOTE Confidence: 0.828827753913044
00:23:19.270 --> 00:23:19.780 Kobe 2,
NOTE Confidence: 0.828827753913044
00:23:19.780 --> 00:23:21.565 So this was a small study of
NOTE Confidence: 0.828827753913044
00:23:21.565 --> 00:23:23.597 just six people by my colleagues
NOTE Confidence: 0.828827753913044
00:23:23.597 --> 00:23:25.500 in Sweden where they looked at
NOTE Confidence: 0.828827753913044
00:23:25.500 --> 00:23:27.064 CSF markers of inflammation,
NOTE Confidence: 0.828827753913044
00:23:27.064 --> 00:23:29.830 and they also try to detect SARS,
NOTE Confidence: 0.828827753913044
00:23:29.830 --> 00:23:31.478 Co V2 by PCR.
NOTE Confidence: 0.828827753913044
00:23:31.478 --> 00:23:33.997 And in this study they found very,
NOTE Confidence: 0.828827753913044
00:23:33.997 --> 00:23:35.731 very low level detection by PCR
NOTE Confidence: 0.828827753913044
00:23:35.731 --> 00:23:37.497 in half of the participants,
NOTE Confidence: 0.828827753913044
00:23:37.500 --> 00:23:38.980 but they essentially felt that
NOTE Confidence: 0.828827753913044

00:23:38.980 --> 00:23:41.020 based on the levels of detection
NOTE Confidence: 0.828827753913044

00:23:41.020 --> 00:23:43.648 and their subsequent work that this
NOTE Confidence: 0.828827753913044

00:23:43.648 --> 00:23:45.400 was probably just contamination
NOTE Confidence: 0.828827753913044

00:23:45.400 --> 00:23:47.941 and they later did a review article
NOTE Confidence: 0.828827753913044

00:23:47.941 --> 00:23:49.846 where they actually looked at all
NOTE Confidence: 0.828827753913044

00:23:49.846 --> 00:23:51.478 of the published reports to date,
NOTE Confidence: 0.828827753913044

00:23:51.480 --> 00:23:54.040 which had been almost 450 reports to date.
NOTE Confidence: 0.828827753913044

00:23:54.040 --> 00:23:56.476 Looking for PCR detection of SARS,
NOTE Confidence: 0.828827753913044

00:23:56.480 --> 00:24:00.332 Co V2 in CSF in people with acute COVID-19,
NOTE Confidence: 0.828827753913044

00:24:00.340 --> 00:24:01.860 mostly with severe disease.
NOTE Confidence: 0.828827753913044

00:24:01.860 --> 00:24:03.760 Almost all with neurologic symptoms,
NOTE Confidence: 0.828827753913044

00:24:03.760 --> 00:24:05.350 which should be the indication
NOTE Confidence: 0.828827753913044

00:24:05.350 --> 00:24:06.812 for lumbar puncture and starts.
NOTE Confidence: 0.828827753913044

00:24:06.812 --> 00:24:08.318 Kovi 2 was only detected in
NOTE Confidence: 0.828827753913044

00:24:08.318 --> 00:24:10.039 less than 3% of those cases,
NOTE Confidence: 0.828827753913044

00:24:10.039 --> 00:24:12.510 so I think this is very convincing

NOTE Confidence: 0.828827753913044

00:24:12.582 --> 00:24:14.616 evidence that direct viral invasion,

NOTE Confidence: 0.828827753913044

00:24:14.616 --> 00:24:16.476 main and and replication within

NOTE Confidence: 0.828827753913044

00:24:16.476 --> 00:24:18.910 the CNS may not be a major

NOTE Confidence: 0.828827753913044

00:24:18.910 --> 00:24:20.214 driver of neurologic symptoms.

NOTE Confidence: 0.828827753913044

00:24:20.220 --> 00:24:20.752 However,

NOTE Confidence: 0.828827753913044

00:24:20.752 --> 00:24:23.944 this study shows elevations of immune

NOTE Confidence: 0.828827753913044

00:24:23.944 --> 00:24:26.220 activation biomarkers in the CSF,

NOTE Confidence: 0.828827753913044

00:24:26.220 --> 00:24:27.505 so similar to the patient

NOTE Confidence: 0.828827753913044

00:24:27.505 --> 00:24:28.790 case that I showed you,

NOTE Confidence: 0.828827753913044

00:24:28.790 --> 00:24:30.850 they found elevation of CSF,

NOTE Confidence: 0.828827753913044

00:24:30.850 --> 00:24:33.534 neopterin and beta microglobulin.

NOTE Confidence: 0.828827753913044

00:24:33.534 --> 00:24:37.102 Myeloid biomarkers of myeloid inflammation in

NOTE Confidence: 0.828827753913044

00:24:37.102 --> 00:24:38.798 all of the individuals that they looked at.

NOTE Confidence: 0.828827753913044

00:24:38.800 --> 00:24:40.678 The dotted line here being the

NOTE Confidence: 0.828827753913044

00:24:40.678 --> 00:24:42.350 normal levels and healthy controls,

NOTE Confidence: 0.828827753913044

00:24:42.350 --> 00:24:44.905 and they also found a hint of
NOTE Confidence: 0.828827753913044

00:24:44.905 --> 00:24:46.866 neuronal injury in a few of
NOTE Confidence: 0.828827753913044

00:24:46.866 --> 00:24:48.396 the people during this time.
NOTE Confidence: 0.828827753913044

00:24:48.400 --> 00:24:50.452 And I'll come back to this in a minute,
NOTE Confidence: 0.828827753913044

00:24:50.460 --> 00:24:53.500 so this was really the first clue that
NOTE Confidence: 0.828827753913044

00:24:53.500 --> 00:24:55.319 that neuroinflammation was predominant.
NOTE Confidence: 0.828827753913044

00:24:55.320 --> 00:24:58.008 Even without detection in viral PCR.
NOTE Confidence: 0.828827753913044

00:24:58.008 --> 00:24:58.336 Now,
NOTE Confidence: 0.828827753913044

00:24:58.336 --> 00:25:00.960 this is a beautiful study led by actually
NOTE Confidence: 0.828827753913044

00:25:01.029 --> 00:25:03.539 today's neurology grand rounds speaker.
NOTE Confidence: 0.828827753913044

00:25:03.540 --> 00:25:05.472 Shibani Mukherjee and colleagues
NOTE Confidence: 0.828827753913044

00:25:05.472 --> 00:25:07.688 from MGH where they looked at
NOTE Confidence: 0.828827753913044

00:25:07.688 --> 00:25:09.560 larger numbers of people so they
NOTE Confidence: 0.828827753913044

00:25:09.621 --> 00:25:11.667 had 27 people and they collected
NOTE Confidence: 0.828827753913044

00:25:11.667 --> 00:25:13.450 CSF during acute COVID-19 again,
NOTE Confidence: 0.828827753913044

00:25:13.450 --> 00:25:15.376 people who had LP's for neurologic

NOTE Confidence: 0.828827753913044

00:25:15.376 --> 00:25:17.553 indications and so this is not a

NOTE Confidence: 0.828827753913044

00:25:17.553 --> 00:25:18.938 survey and everyone with COVID,

NOTE Confidence: 0.828827753913044

00:25:18.940 --> 00:25:20.998 but it's actually people who had

NOTE Confidence: 0.828827753913044

00:25:20.998 --> 00:25:23.140 distinct neurologic disease and they did.

NOTE Confidence: 0.828827753913044

00:25:23.140 --> 00:25:24.990 QT PCR and metagenomic sequencing

NOTE Confidence: 0.828827753913044

00:25:24.990 --> 00:25:27.439 in all 27 samples and did not

NOTE Confidence: 0.828827753913044

00:25:27.439 --> 00:25:29.727 find detection of SARS Co V2 in

NOTE Confidence: 0.828827753913044

00:25:29.727 --> 00:25:30.867 any of the samples.

NOTE Confidence: 0.828827753913044

00:25:30.870 --> 00:25:31.336 However,

NOTE Confidence: 0.828827753913044

00:25:31.336 --> 00:25:34.598 they did find elevation of CSF inflammatory.

NOTE Confidence: 0.828827753913044

00:25:34.600 --> 00:25:37.025 Markers in the COVID-19 patients

NOTE Confidence: 0.828827753913044

00:25:37.025 --> 00:25:40.320 that are shown with the red dots,

NOTE Confidence: 0.828827753913044

00:25:40.320 --> 00:25:42.378 particularly a couple of the markers,

NOTE Confidence: 0.735505144285714

00:25:42.380 --> 00:25:48.925 including MCP one and CSF mcglen beta,

NOTE Confidence: 0.735505144285714

00:25:48.930 --> 00:25:53.234 compared to healthy controls I wanna I'll 6.

NOTE Confidence: 0.735505144285714

00:25:53.240 --> 00:25:54.806 And interestingly, in this study they
NOTE Confidence: 0.735505144285714

00:25:54.806 --> 00:25:56.421 also looked at other viral infections
NOTE Confidence: 0.735505144285714

00:25:56.421 --> 00:25:58.248 and compared the levels here in West
NOTE Confidence: 0.735505144285714

00:25:58.248 --> 00:26:00.069 Nile virus was the only one that had
NOTE Confidence: 0.735505144285714

00:26:00.069 --> 00:26:01.904 higher levels in some of these markers.
NOTE Confidence: 0.735505144285714

00:26:01.904 --> 00:26:03.304 So again, this is suggesting and
NOTE Confidence: 0.735505144285714

00:26:03.304 --> 00:26:04.804 I should say that most of these
NOTE Confidence: 0.735505144285714

00:26:04.804 --> 00:26:06.280 people had normal CSF white counts,
NOTE Confidence: 0.735505144285714

00:26:06.280 --> 00:26:07.884 so they didn't have.
NOTE Confidence: 0.735505144285714

00:26:07.884 --> 00:26:09.889 Will work evidence of Pleocytosis,
NOTE Confidence: 0.735505144285714

00:26:09.890 --> 00:26:11.800 but they had subtle neuroinflammation.
NOTE Confidence: 0.85082046875

00:26:13.920 --> 00:26:15.768 Interestingly, there has been
NOTE Confidence: 0.85082046875

00:26:15.768 --> 00:26:18.540 look at other types of markers
NOTE Confidence: 0.85082046875

00:26:18.621 --> 00:26:21.009 in CSF in acute COVID patients,
NOTE Confidence: 0.85082046875

00:26:21.010 --> 00:26:22.774 and this paper was recently published
NOTE Confidence: 0.85082046875

00:26:22.774 --> 00:26:25.075 in about a lot of attention because

NOTE Confidence: 0.85082046875

00:26:25.075 --> 00:26:26.855 it demonstrates the fact that

NOTE Confidence: 0.85082046875

00:26:26.855 --> 00:26:29.018 markers that are associated with

NOTE Confidence: 0.85082046875

00:26:29.018 --> 00:26:30.874 neurodegeneration in Alzheimer's disease

NOTE Confidence: 0.85082046875

00:26:30.874 --> 00:26:32.854 were actually abnormal in people

NOTE Confidence: 0.85082046875

00:26:32.854 --> 00:26:34.942 who had COVID were hospitalized with

NOTE Confidence: 0.85082046875

00:26:34.942 --> 00:26:37.067 acute COVID and neurologic symptoms.

NOTE Confidence: 0.85082046875

00:26:37.070 --> 00:26:38.732 So again, here are the COVID

NOTE Confidence: 0.85082046875

00:26:38.732 --> 00:26:40.510 patients are shown in the orange,

NOTE Confidence: 0.85082046875

00:26:40.510 --> 00:26:43.720 and it's showing reductions in soluble.

NOTE Confidence: 0.85082046875

00:26:43.720 --> 00:26:46.290 A panel of precursor protein

NOTE Confidence: 0.85082046875

00:26:46.290 --> 00:26:49.368 and amyloid beta in people with

NOTE Confidence: 0.85082046875

00:26:49.368 --> 00:26:51.420 COVID-19 during acute disease.

NOTE Confidence: 0.85082046875

00:26:51.420 --> 00:26:52.818 This has been a little bit

NOTE Confidence: 0.85082046875

00:26:52.818 --> 00:26:54.282 interpreted to say that maybe this

NOTE Confidence: 0.85082046875

00:26:54.282 --> 00:26:55.716 is setting these people up for

NOTE Confidence: 0.85082046875

00:26:55.720 --> 00:26:56.806 Alzheimer's type neurodegeneration,
NOTE Confidence: 0.85082046875

00:26:56.806 --> 00:26:58.616 but I was interpret this
NOTE Confidence: 0.85082046875

00:26:58.616 --> 00:27:00.160 to say that actually,
NOTE Confidence: 0.85082046875

00:27:00.160 --> 00:27:02.720 in most acute infectious,
NOTE Confidence: 0.85082046875

00:27:02.720 --> 00:27:04.640 acute viral conditions,
NOTE Confidence: 0.85082046875

00:27:04.640 --> 00:27:06.502 you can see these kinds of changes
NOTE Confidence: 0.85082046875

00:27:06.502 --> 00:27:08.231 that resolve after acute infection and
NOTE Confidence: 0.85082046875

00:27:08.231 --> 00:27:10.268 this is something that we've also seen
NOTE Confidence: 0.85082046875

00:27:10.328 --> 00:27:12.188 and published in acute HIV infection,
NOTE Confidence: 0.85082046875

00:27:12.190 --> 00:27:14.050 so hopefully this doesn't actually.
NOTE Confidence: 0.85082046875

00:27:14.050 --> 00:27:15.820 Mean that there are going
NOTE Confidence: 0.85082046875

00:27:15.820 --> 00:27:17.236 to be Alzheimer's disease.
NOTE Confidence: 0.85082046875

00:27:17.240 --> 00:27:19.186 You know Avalanche coming in our future.
NOTE Confidence: 0.85082046875

00:27:19.190 --> 00:27:21.314 Although we can talk about that at the end,
NOTE Confidence: 0.85082046875

00:27:21.320 --> 00:27:23.826 but I think that these kinds of
NOTE Confidence: 0.85082046875

00:27:23.826 --> 00:27:26.010 perturbations and amyloid processing and

NOTE Confidence: 0.85082046875

00:27:26.010 --> 00:27:28.262 neuronal processes maybe something better.

NOTE Confidence: 0.85082046875

00:27:28.262 --> 00:27:30.282 Hint that there's been some

NOTE Confidence: 0.85082046875

00:27:30.282 --> 00:27:32.149 injury during acute infection.

NOTE Confidence: 0.85082046875

00:27:32.150 --> 00:27:34.150 So this is really elegant work and this

NOTE Confidence: 0.85082046875

00:27:34.150 --> 00:27:36.006 is being led by my colleague here.

NOTE Confidence: 0.85082046875

00:27:36.010 --> 00:27:36.828 Shelly Farhadian,

NOTE Confidence: 0.85082046875

00:27:36.828 --> 00:27:39.691 who is a faculty member in infectious

NOTE Confidence: 0.85082046875

00:27:39.691 --> 00:27:41.804 disease who's also really a

NOTE Confidence: 0.85082046875

00:27:41.804 --> 00:27:43.440 stellar investigator and clinician

NOTE Confidence: 0.85082046875

00:27:43.440 --> 00:27:45.560 in neuro infectious disease.

NOTE Confidence: 0.85082046875

00:27:45.560 --> 00:27:47.795 And Shelly really took forward

NOTE Confidence: 0.85082046875

00:27:47.795 --> 00:27:49.583 the opportunity to characterize

NOTE Confidence: 0.85082046875

00:27:49.583 --> 00:27:51.270 in a research level,

NOTE Confidence: 0.85082046875

00:27:51.270 --> 00:27:53.188 some of the clinical patients that we're

NOTE Confidence: 0.85082046875

00:27:53.188 --> 00:27:55.490 seeing on the Neuro COVID console service.

NOTE Confidence: 0.85082046875

00:27:55.490 --> 00:27:58.298 So when patients did have CSF
NOTE Confidence: 0.85082046875

00:27:58.298 --> 00:28:00.170 collection for clinical reasons,
NOTE Confidence: 0.85082046875

00:28:00.170 --> 00:28:02.280 Shelly scrambled to do, really.
NOTE Confidence: 0.85082046875

00:28:02.280 --> 00:28:04.260 Real time studies on the CSF,
NOTE Confidence: 0.85082046875

00:28:04.260 --> 00:28:05.820 including things like single cell RNA,
NOTE Confidence: 0.85082046875

00:28:05.820 --> 00:28:08.228 seek on fresh samples to try to
NOTE Confidence: 0.85082046875

00:28:08.228 --> 00:28:10.052 characterize in great detail what
NOTE Confidence: 0.85082046875

00:28:10.052 --> 00:28:11.867 some of the immune perturbations
NOTE Confidence: 0.85082046875

00:28:11.867 --> 00:28:14.000 might be in these patients.
NOTE Confidence: 0.85082046875

00:28:14.000 --> 00:28:16.928 And so in this first six
NOTE Confidence: 0.85082046875

00:28:16.928 --> 00:28:18.880 patients that were evaluated,
NOTE Confidence: 0.85082046875

00:28:18.880 --> 00:28:20.650 they she and other colleagues
NOTE Confidence: 0.85082046875

00:28:20.650 --> 00:28:22.560 here at Yale looked for stars.
NOTE Confidence: 0.85082046875

00:28:22.560 --> 00:28:23.760 Kobe 2 by PCR,
NOTE Confidence: 0.85082046875

00:28:23.760 --> 00:28:25.392 metagenomics and culture did
NOTE Confidence: 0.85082046875

00:28:25.392 --> 00:28:27.840 not find any evidence of virus,

NOTE Confidence: 0.85082046875

00:28:27.840 --> 00:28:29.930 but did find really intriguing

NOTE Confidence: 0.85082046875

00:28:29.930 --> 00:28:32.350 alternate immune responses in the CSF.

NOTE Confidence: 0.85082046875

00:28:32.350 --> 00:28:33.846 And what we did is that we looked

NOTE Confidence: 0.85082046875

00:28:33.846 --> 00:28:35.262 at the patients who had COVID-19

NOTE Confidence: 0.85082046875

00:28:35.262 --> 00:28:36.507 and again on the left.

NOTE Confidence: 0.85082046875

00:28:36.510 --> 00:28:38.358 These are shown in purple compared

NOTE Confidence: 0.85082046875

00:28:38.358 --> 00:28:40.261 them to pre pandemic CSF and

NOTE Confidence: 0.85082046875

00:28:40.261 --> 00:28:42.079 blood controls that we had been

NOTE Confidence: 0.85082046875

00:28:42.079 --> 00:28:43.530 collecting for other studies.

NOTE Confidence: 0.85082046875

00:28:43.530 --> 00:28:45.828 Healthy people who were age matched

NOTE Confidence: 0.85082046875

00:28:45.830 --> 00:28:47.522 and what she found was increased

NOTE Confidence: 0.85082046875

00:28:47.522 --> 00:28:49.322 CSF cytokines in the CSF compared

NOTE Confidence: 0.85082046875

00:28:49.322 --> 00:28:50.246 to the controls.

NOTE Confidence: 0.85082046875

00:28:50.250 --> 00:28:51.805 But what was really interesting

NOTE Confidence: 0.85082046875

00:28:51.805 --> 00:28:53.741 here is that she specifically found

NOTE Confidence: 0.85082046875

00:28:53.741 --> 00:28:55.697 a distinct pattern between the CSF
NOTE Confidence: 0.85082046875

00:28:55.697 --> 00:28:57.499 cytokine elevations and those in blood,
NOTE Confidence: 0.85082046875

00:28:57.500 --> 00:28:59.165 suggesting that there was actually
NOTE Confidence: 0.85082046875

00:28:59.165 --> 00:29:00.164 a compartmentalized response.
NOTE Confidence: 0.85082046875

00:29:00.170 --> 00:29:01.758 This wasn't necessarily just
NOTE Confidence: 0.85082046875

00:29:01.758 --> 00:29:03.346 a spillover of inflammation.
NOTE Confidence: 0.85082046875

00:29:03.350 --> 00:29:04.496 Systemic circulation,
NOTE Confidence: 0.85082046875

00:29:04.496 --> 00:29:07.361 but instead was actually potentially
NOTE Confidence: 0.85082046875

00:29:07.361 --> 00:29:10.703 a local response related to local
NOTE Confidence: 0.85082046875

00:29:10.703 --> 00:29:12.755 cells and local perturbations.
NOTE Confidence: 0.85082046875

00:29:12.760 --> 00:29:14.235 Another thing that she detected
NOTE Confidence: 0.85082046875

00:29:14.235 --> 00:29:16.461 by single cell RNA seq was a
NOTE Confidence: 0.85082046875

00:29:16.461 --> 00:29:17.157 increased frequency.
NOTE Confidence: 0.817463569444445

00:29:17.160 --> 00:29:20.229 B cells in the CSF and so this led
NOTE Confidence: 0.817463569444445

00:29:20.229 --> 00:29:22.936 to an interrogation of antibody
NOTE Confidence: 0.817463569444445

00:29:22.936 --> 00:29:25.848 responses in the CSF and really,

NOTE Confidence: 0.817463569444445
00:29:25.848 --> 00:29:26.820 really interesting work.
NOTE Confidence: 0.817463569444445
00:29:26.820 --> 00:29:29.459 Again led by Shelly and other colleagues
NOTE Confidence: 0.817463569444445
00:29:29.459 --> 00:29:32.880 here at Yale and also collaborators at UCSF.
NOTE Confidence: 0.817463569444445
00:29:32.880 --> 00:29:35.040 Using some really novel ways to
NOTE Confidence: 0.817463569444445
00:29:35.040 --> 00:29:37.220 detect whole panels of anti SARS,
NOTE Confidence: 0.817463569444445
00:29:37.220 --> 00:29:38.192 Kobe 2 antibodies.
NOTE Confidence: 0.817463569444445
00:29:38.192 --> 00:29:40.460 They were able to describe the fact
NOTE Confidence: 0.817463569444445
00:29:40.520 --> 00:29:42.704 that anti SARS Co V2 antibodies were
NOTE Confidence: 0.817463569444445
00:29:42.704 --> 00:29:45.260 detected in CSF and all of these patients,
NOTE Confidence: 0.817463569444445
00:29:45.260 --> 00:29:47.000 but actually some of the antibodies
NOTE Confidence: 0.817463569444445
00:29:47.000 --> 00:29:48.769 were distinct from the patterns of
NOTE Confidence: 0.817463569444445
00:29:48.769 --> 00:29:50.419 the antibodies that were found in
NOTE Confidence: 0.817463569444445
00:29:50.419 --> 00:29:52.079 the blood in the same patients.
NOTE Confidence: 0.817463569444445
00:29:52.080 --> 00:29:53.079 And in fact,
NOTE Confidence: 0.817463569444445
00:29:53.079 --> 00:29:54.744 when some of these antibodies
NOTE Confidence: 0.817463569444445

00:29:54.744 --> 00:29:56.840 remain into monoclonal antibodies,
NOTE Confidence: 0.817463569444445

00:29:56.840 --> 00:30:00.032 they were found in a novel auto
NOTE Confidence: 0.817463569444445

00:30:00.032 --> 00:30:02.047 antibody discovery method to
NOTE Confidence: 0.817463569444445

00:30:02.047 --> 00:30:03.727 actually be autoreactive.
NOTE Confidence: 0.817463569444445

00:30:03.730 --> 00:30:04.969 To brain tissue.
NOTE Confidence: 0.817463569444445

00:30:04.969 --> 00:30:07.458 So these are again hints that
NOTE Confidence: 0.817463569444445

00:30:07.458 --> 00:30:09.954 not only is there a generalized
NOTE Confidence: 0.817463569444445

00:30:09.954 --> 00:30:11.890 neuroinflammation and antibody formation,
NOTE Confidence: 0.817463569444445

00:30:11.890 --> 00:30:14.067 but some of these antibodies that are
NOTE Confidence: 0.817463569444445

00:30:14.067 --> 00:30:15.988 developing maybe in response to SARS,
NOTE Confidence: 0.817463569444445

00:30:15.990 --> 00:30:18.510 Co V2 are actually auto reacting or
NOTE Confidence: 0.817463569444445

00:30:18.510 --> 00:30:20.019 autoimmune antibodies that could
NOTE Confidence: 0.817463569444445

00:30:20.019 --> 00:30:21.859 be attacking the nervous system.
NOTE Confidence: 0.863128735

00:30:24.060 --> 00:30:26.460 So what have we learned from autopsy tissue?
NOTE Confidence: 0.863128735

00:30:26.460 --> 00:30:28.140 And I think that this is again,
NOTE Confidence: 0.863128735

00:30:28.140 --> 00:30:29.376 it's come out and fix and

NOTE Confidence: 0.863128735

00:30:29.376 --> 00:30:30.699 starts over the last two years.

NOTE Confidence: 0.863128735

00:30:30.700 --> 00:30:33.322 Is these autopsy series looking at

NOTE Confidence: 0.863128735

00:30:33.322 --> 00:30:36.350 people who died with acute COVID-19?

NOTE Confidence: 0.863128735

00:30:36.350 --> 00:30:37.122 Always have of course,

NOTE Confidence: 0.863128735

00:30:37.122 --> 00:30:38.762 all the caveats of the fact that they

NOTE Confidence: 0.863128735

00:30:38.762 --> 00:30:40.070 will affect people who have really,

NOTE Confidence: 0.863128735

00:30:40.070 --> 00:30:43.269 really severe disease who died from COVID.

NOTE Confidence: 0.863128735

00:30:43.270 --> 00:30:44.845 And many of these people

NOTE Confidence: 0.863128735

00:30:44.845 --> 00:30:46.105 had prolonged ICU stays.

NOTE Confidence: 0.863128735

00:30:46.110 --> 00:30:47.688 Many of them had, you know,

NOTE Confidence: 0.863128735

00:30:47.690 --> 00:30:49.490 hypertension, heart failure, hypoxemia,

NOTE Confidence: 0.863128735

00:30:49.490 --> 00:30:52.830 and you can see here for example.

NOTE Confidence: 0.863128735

00:30:52.830 --> 00:30:55.182 This is a group of patients that

NOTE Confidence: 0.863128735

00:30:55.182 --> 00:30:57.570 were collected again at MGH.

NOTE Confidence: 0.863128735

00:30:57.570 --> 00:30:58.710 18 people.

NOTE Confidence: 0.863128735

00:30:58.710 --> 00:31:01.629 Most of these people did not have
NOTE Confidence: 0.863128735

00:31:01.629 --> 00:31:02.880 significant neurological symptoms,
NOTE Confidence: 0.863128735

00:31:02.880 --> 00:31:04.390 but they, but they died.
NOTE Confidence: 0.863128735

00:31:04.390 --> 00:31:06.160 All of them had hypoxic ischemic
NOTE Confidence: 0.863128735

00:31:06.160 --> 00:31:07.340 injury in the brain.
NOTE Confidence: 0.863128735

00:31:07.340 --> 00:31:09.363 But I think what's important in this
NOTE Confidence: 0.863128735

00:31:09.363 --> 00:31:11.805 study is that this study was particularly
NOTE Confidence: 0.863128735

00:31:11.805 --> 00:31:13.700 looking for detection of virus,
NOTE Confidence: 0.863128735

00:31:13.700 --> 00:31:15.536 and they did different methods of
NOTE Confidence: 0.863128735

00:31:15.536 --> 00:31:17.084 detection trying to determine whether
NOTE Confidence: 0.863128735

00:31:17.084 --> 00:31:18.710 or not there was actually SARS.
NOTE Confidence: 0.863128735

00:31:18.710 --> 00:31:20.775 Kobe 2IN the brains of these people
NOTE Confidence: 0.863128735

00:31:20.775 --> 00:31:23.225 who were very very severely ill with
NOTE Confidence: 0.863128735

00:31:23.225 --> 00:31:24.484 COVID-19 using immunohistochemistry.
NOTE Confidence: 0.863128735

00:31:24.484 --> 00:31:27.578 They did not detect virus in neurons,
NOTE Confidence: 0.863128735

00:31:27.580 --> 00:31:28.504 glial and ileum,

NOTE Confidence: 0.863128735

00:31:28.504 --> 00:31:30.660 or immune cells in any structures of

NOTE Confidence: 0.863128735

00:31:30.719 --> 00:31:33.430 the brain. In any of these individuals.

NOTE Confidence: 0.863128735

00:31:33.430 --> 00:31:36.182 When they used PCR and looking just for

NOTE Confidence: 0.863128735

00:31:36.182 --> 00:31:38.589 fragments of the nucleocapsid protein,

NOTE Confidence: 0.863128735

00:31:38.590 --> 00:31:40.186 they did find positive findings in

NOTE Confidence: 0.863128735

00:31:40.186 --> 00:31:42.293 six of the 52 different blocks that

NOTE Confidence: 0.863128735

00:31:42.293 --> 00:31:44.582 they looked at and sort of equivocal.

NOTE Confidence: 0.863128735

00:31:44.590 --> 00:31:46.570 Very low, low level findings,

NOTE Confidence: 0.863128735

00:31:46.570 --> 00:31:48.538 and in some this is consistent

NOTE Confidence: 0.863128735

00:31:48.538 --> 00:31:49.522 with other studies.

NOTE Confidence: 0.863128735

00:31:49.530 --> 00:31:50.934 There's also a really nice study

NOTE Confidence: 0.863128735

00:31:50.934 --> 00:31:53.141 out of the NIH that also looked at a

NOTE Confidence: 0.863128735

00:31:53.141 --> 00:31:54.877 number of people that again did not

NOTE Confidence: 0.863128735

00:31:54.877 --> 00:31:58.470 detect intact virus in any of the patients,

NOTE Confidence: 0.863128735

00:31:58.470 --> 00:32:00.138 so this would suggest again that

NOTE Confidence: 0.863128735

00:32:00.138 --> 00:32:01.610 if you had replicating virus,
NOTE Confidence: 0.863128735

00:32:01.610 --> 00:32:02.510 typical viral encephalitis.
NOTE Confidence: 0.863128735

00:32:02.510 --> 00:32:04.610 You find a lot of intact virus,
NOTE Confidence: 0.863128735

00:32:04.610 --> 00:32:06.540 and that's not being found.
NOTE Confidence: 0.863128735

00:32:06.540 --> 00:32:08.724 This is another study in another group.
NOTE Confidence: 0.863128735

00:32:08.730 --> 00:32:11.674 This is a group out of Germany that
NOTE Confidence: 0.863128735

00:32:11.674 --> 00:32:13.841 has published reports suggesting that
NOTE Confidence: 0.863128735

00:32:13.841 --> 00:32:17.600 they can detect intact virus in some people,
NOTE Confidence: 0.863128735

00:32:17.600 --> 00:32:19.060 but but what's really remarkable
NOTE Confidence: 0.863128735

00:32:19.060 --> 00:32:21.278 about this study is the the widespread
NOTE Confidence: 0.863128735

00:32:21.278 --> 00:32:23.714 inflammation that was reported in this study.
NOTE Confidence: 0.863128735

00:32:23.720 --> 00:32:24.492 So again,
NOTE Confidence: 0.863128735

00:32:24.492 --> 00:32:27.194 this is autopsy data from 43 patients.
NOTE Confidence: 0.863128735

00:32:27.200 --> 00:32:29.876 Each column in this figure is
NOTE Confidence: 0.863128735

00:32:29.876 --> 00:32:32.260 showing you the the demographic
NOTE Confidence: 0.863128735

00:32:32.260 --> 00:32:34.860 information for an individual donor

NOTE Confidence: 0.863128735

00:32:34.860 --> 00:32:37.750 who died of acute COVID-19.

NOTE Confidence: 0.863128735

00:32:37.750 --> 00:32:40.279 And then you can see on the left the

NOTE Confidence: 0.863128735

00:32:40.279 --> 00:32:42.197 different brain regions that were

NOTE Confidence: 0.863128735

00:32:42.197 --> 00:32:44.275 examined and what this large portion

NOTE Confidence: 0.863128735

00:32:44.275 --> 00:32:46.893 of the chart is showing is microglial

NOTE Confidence: 0.863128735

00:32:46.893 --> 00:32:49.473 activation widespread in the brains of

NOTE Confidence: 0.863128735

00:32:49.473 --> 00:32:52.187 almost every single one of these donors?

NOTE Confidence: 0.863128735

00:32:52.190 --> 00:32:53.738 So microglial activation there

NOTE Confidence: 0.863128735

00:32:53.738 --> 00:32:56.060 was also a very similar graph

NOTE Confidence: 0.863128735

00:32:56.129 --> 00:32:58.306 shown for CD8T cell infiltration.

NOTE Confidence: 0.863128735

00:32:58.306 --> 00:32:59.370 Now again,

NOTE Confidence: 0.863128735

00:32:59.370 --> 00:33:02.170 in the setting of acute illness and death,

NOTE Confidence: 0.863128735

00:33:02.170 --> 00:33:04.006 all sorts of hypoxic ischemic injury.

NOTE Confidence: 0.863128735

00:33:04.010 --> 00:33:06.368 Maybe we expect some microglial activation,

NOTE Confidence: 0.863128735

00:33:06.370 --> 00:33:07.660 but this seemed to be to.

NOTE Confidence: 0.863128735

00:33:07.660 --> 00:33:09.184 This pathology group seem to be
NOTE Confidence: 0.863128735

00:33:09.184 --> 00:33:10.782 way out of proportion to what
NOTE Confidence: 0.863128735

00:33:10.782 --> 00:33:11.838 they would have expected,
NOTE Confidence: 0.863128735

00:33:11.840 --> 00:33:14.328 and compared to other types of donors who
NOTE Confidence: 0.863128735

00:33:14.328 --> 00:33:17.058 also of course died with acute illnesses
NOTE Confidence: 0.86507961826087

00:33:17.060 --> 00:33:18.350 and everything in this graph
NOTE Confidence: 0.86507961826087

00:33:18.350 --> 00:33:20.678 that is not blue is shown to be
NOTE Confidence: 0.86507961826087

00:33:20.678 --> 00:33:21.990 abnormal microglial activation in
NOTE Confidence: 0.86507961826087

00:33:21.990 --> 00:33:23.780 the bottom part of the figure.
NOTE Confidence: 0.86507961826087

00:33:23.780 --> 00:33:26.784 I'm showing you in purple the few
NOTE Confidence: 0.86507961826087

00:33:26.784 --> 00:33:28.596 brains in which they could base.
NOTE Confidence: 0.86507961826087

00:33:28.600 --> 00:33:31.440 They identified stars Kobe 2 RNA or in
NOTE Confidence: 0.86507961826087

00:33:31.440 --> 00:33:34.576 a few more brains of positive SARS.
NOTE Confidence: 0.86507961826087

00:33:34.580 --> 00:33:37.268 Co V2 proteins such as nucleocapsid
NOTE Confidence: 0.86507961826087

00:33:37.268 --> 00:33:38.612 or spike protein.
NOTE Confidence: 0.86507961826087

00:33:38.620 --> 00:33:40.360 And what's really remarkable here

NOTE Confidence: 0.86507961826087
00:33:40.360 --> 00:33:42.934 is that the high levels of neural
NOTE Confidence: 0.86507961826087
00:33:42.934 --> 00:33:44.474 inflammation do not necessarily
NOTE Confidence: 0.86507961826087
00:33:44.474 --> 00:33:46.466 cluster only in those people
NOTE Confidence: 0.86507961826087
00:33:46.466 --> 00:33:48.030 who had detectable virus,
NOTE Confidence: 0.86507961826087
00:33:48.030 --> 00:33:49.976 but in fact is widespread even in
NOTE Confidence: 0.86507961826087
00:33:49.976 --> 00:33:51.859 people with no detectable virus.
NOTE Confidence: 0.86507961826087
00:33:51.860 --> 00:33:54.668 So again, what's been emerging is
NOTE Confidence: 0.86507961826087
00:33:54.668 --> 00:33:56.540 high levels of neuroinflammation.
NOTE Confidence: 0.86507961826087
00:33:56.540 --> 00:33:59.557 In the absence of major viral replication.
NOTE Confidence: 0.86507961826087
00:33:59.560 --> 00:34:00.918 And this is one more study that
NOTE Confidence: 0.86507961826087
00:34:00.918 --> 00:34:01.500 I just revealed.
NOTE Confidence: 0.86507961826087
00:34:01.500 --> 00:34:02.412 One more thing,
NOTE Confidence: 0.86507961826087
00:34:02.412 --> 00:34:04.236 I think that's truly important about
NOTE Confidence: 0.86507961826087
00:34:04.236 --> 00:34:06.058 the neuropathology of COVID-19.
NOTE Confidence: 0.86507961826087
00:34:06.060 --> 00:34:07.676 Again, an autopsy study.
NOTE Confidence: 0.86507961826087

00:34:07.676 --> 00:34:11.139 Many of these people died with sudden death,
NOTE Confidence: 0.86507961826087

00:34:11.140 --> 00:34:13.492 so they were cases of people
NOTE Confidence: 0.86507961826087

00:34:13.492 --> 00:34:15.060 who were corner cases,
NOTE Confidence: 0.86507961826087

00:34:15.060 --> 00:34:18.730 so they weren't necessarily hospitalized.
NOTE Confidence: 0.86507961826087

00:34:18.730 --> 00:34:22.032 These individuals did not have any other
NOTE Confidence: 0.86507961826087

00:34:22.032 --> 00:34:23.837 kind of major respiratory findings.
NOTE Confidence: 0.86507961826087

00:34:23.840 --> 00:34:27.263 They did not have any overt strokes,
NOTE Confidence: 0.86507961826087

00:34:27.263 --> 00:34:29.849 but when brain tissue from these
NOTE Confidence: 0.86507961826087

00:34:29.849 --> 00:34:31.954 individuals was examined both by
NOTE Confidence: 0.86507961826087

00:34:31.954 --> 00:34:34.306 11 Tesla and Mirai autopsy tissue,
NOTE Confidence: 0.86507961826087

00:34:34.310 --> 00:34:37.250 as well as by histopathologic examination.
NOTE Confidence: 0.86507961826087

00:34:37.250 --> 00:34:40.386 They were found to have microvascular injury,
NOTE Confidence: 0.86507961826087

00:34:40.390 --> 00:34:43.575 so if fibrinogen leakage from
NOTE Confidence: 0.86507961826087

00:34:43.575 --> 00:34:45.486 blood vessels microhemorrhages.
NOTE Confidence: 0.86507961826087

00:34:45.490 --> 00:34:47.910 And large collections of perivascular
NOTE Confidence: 0.86507961826087

00:34:47.910 --> 00:34:51.503 macrophages so the the hint here was that

NOTE Confidence: 0.86507961826087

00:34:51.503 --> 00:34:54.730 even in people who don't have overt strokes,

NOTE Confidence: 0.86507961826087

00:34:54.730 --> 00:34:56.110 microvascular injury microvascular

NOTE Confidence: 0.86507961826087

00:34:56.110 --> 00:34:59.330 changes may be also underlying some of

NOTE Confidence: 0.86507961826087

00:34:59.393 --> 00:35:01.811 the neurologic types of consequences that

NOTE Confidence: 0.86507961826087

00:35:01.811 --> 00:35:04.750 we're seeing in people with acute COVID-19.

NOTE Confidence: 0.86507961826087

00:35:04.750 --> 00:35:05.025 Again,

NOTE Confidence: 0.86507961826087

00:35:05.025 --> 00:35:06.675 this study did not detect SARS

NOTE Confidence: 0.86507961826087

00:35:06.675 --> 00:35:08.849 Co V2 in any of their brains

NOTE Confidence: 0.86507961826087

00:35:08.849 --> 00:35:10.781 segments looked at and this group.

NOTE Confidence: 0.86507961826087

00:35:10.790 --> 00:35:13.002 This is from a group of based

NOTE Confidence: 0.86507961826087

00:35:13.002 --> 00:35:13.950 primarily at NIH.

NOTE Confidence: 0.86507961826087

00:35:13.950 --> 00:35:16.278 They continue to do studies and do not.

NOTE Confidence: 0.86507961826087

00:35:16.280 --> 00:35:18.770 Find any virus in the brain.

NOTE Confidence: 0.86507961826087

00:35:18.770 --> 00:35:21.137 So I I think the final thing to talk

NOTE Confidence: 0.86507961826087

00:35:21.137 --> 00:35:23.531 about in terms of pathology are some

NOTE Confidence: 0.86507961826087

00:35:23.531 --> 00:35:25.480 of these neuronal injury markers.
NOTE Confidence: 0.86507961826087

00:35:25.480 --> 00:35:27.840 So I mentioned neuroinflammation.
NOTE Confidence: 0.86507961826087

00:35:27.840 --> 00:35:30.290 I mentioned the fact that there doesn't
NOTE Confidence: 0.86507961826087

00:35:30.290 --> 00:35:32.210 seem to be robust active replication,
NOTE Confidence: 0.86507961826087

00:35:32.210 --> 00:35:34.910 but there may be microvascular injury,
NOTE Confidence: 0.86507961826087

00:35:34.910 --> 00:35:37.022 but is there actually brain injury
NOTE Confidence: 0.86507961826087

00:35:37.022 --> 00:35:39.209 in these patients during acute COVID?
NOTE Confidence: 0.86507961826087

00:35:39.210 --> 00:35:40.302 And this is a little bit of
NOTE Confidence: 0.86507961826087

00:35:40.302 --> 00:35:41.609 a of a concerning study,
NOTE Confidence: 0.86507961826087

00:35:41.610 --> 00:35:43.794 I think we have a lot more information
NOTE Confidence: 0.86507961826087

00:35:43.794 --> 00:35:45.469 that we need to look into,
NOTE Confidence: 0.86507961826087

00:35:45.470 --> 00:35:48.046 but this is a group that had large
NOTE Confidence: 0.86507961826087

00:35:48.046 --> 00:35:50.919 numbers of people who had acute COVID-19.
NOTE Confidence: 0.86507961826087

00:35:50.920 --> 00:35:53.797 So 246 people who were hospitalized with
NOTE Confidence: 0.86507961826087

00:35:53.797 --> 00:35:56.748 acute COVID-19 this is from NYU in New York.
NOTE Confidence: 0.86507961826087

00:35:56.750 --> 00:35:59.042 And samples were collected from the

NOTE Confidence: 0.86507961826087

00:35:59.042 --> 00:36:01.386 blood for these individuals and then

NOTE Confidence: 0.86507961826087

00:36:01.386 --> 00:36:03.266 highly sensitive assays were used

NOTE Confidence: 0.86507961826087

00:36:03.266 --> 00:36:05.170 to measure neuronal injury markers

NOTE Confidence: 0.86507961826087

00:36:05.170 --> 00:36:07.306 that are leaking into the blood.

NOTE Confidence: 0.86507961826087

00:36:07.310 --> 00:36:08.590 So these include neurofilament

NOTE Confidence: 0.86507961826087

00:36:08.590 --> 00:36:09.550 light chain was,

NOTE Confidence: 0.86507961826087

00:36:09.550 --> 00:36:11.608 which is a biomarker of axonal injury.

NOTE Confidence: 0.86507961826087

00:36:11.610 --> 00:36:13.030 Glial fibrillary acid protein,

NOTE Confidence: 0.86507961826087

00:36:13.030 --> 00:36:15.160 which is a marker of astrocyte

NOTE Confidence: 0.86507961826087

00:36:15.221 --> 00:36:17.946 injury and ECHL one which is also

NOTE Confidence: 0.86507961826087

00:36:17.946 --> 00:36:20.200 a neuron specific protein and what

NOTE Confidence: 0.86507961826087

00:36:20.200 --> 00:36:22.545 this group found was that NFL and

NOTE Confidence: 0.86507961826087

00:36:22.545 --> 00:36:25.191 GF AP were quite elevated in the

NOTE Confidence: 0.86507961826087

00:36:25.191 --> 00:36:26.679 blood in these acute

NOTE Confidence: 0.786990786590909

00:36:26.762 --> 00:36:27.880 COVID patients.

NOTE Confidence: 0.786990786590909

00:36:27.880 --> 00:36:29.915 These were not necessarily people
NOTE Confidence: 0.786990786590909

00:36:29.915 --> 00:36:31.543 who had neurologic conditions,
NOTE Confidence: 0.786990786590909

00:36:31.550 --> 00:36:34.274 they just took all comers and what
NOTE Confidence: 0.786990786590909

00:36:34.274 --> 00:36:36.259 was interesting was that these
NOTE Confidence: 0.786990786590909

00:36:36.259 --> 00:36:38.474 measures were actually quite a bit
NOTE Confidence: 0.786990786590909

00:36:38.474 --> 00:36:40.394 higher than even those found in
NOTE Confidence: 0.786990786590909

00:36:40.394 --> 00:36:42.378 people with Alzheimer's disease.
NOTE Confidence: 0.786990786590909

00:36:42.380 --> 00:36:43.985 So again, what the implications
NOTE Confidence: 0.786990786590909

00:36:43.985 --> 00:36:46.077 of this might be for people
NOTE Confidence: 0.786990786590909

00:36:46.077 --> 00:36:47.757 who survive acute COVID-19,
NOTE Confidence: 0.786990786590909

00:36:47.760 --> 00:36:49.538 I think is a really important question,
NOTE Confidence: 0.786990786590909

00:36:49.540 --> 00:36:51.880 but it's a really clinically unknown
NOTE Confidence: 0.786990786590909

00:36:51.880 --> 00:36:54.064 and I will say that during acute
NOTE Confidence: 0.786990786590909

00:36:54.064 --> 00:36:56.067 HIV infection we also see elevations
NOTE Confidence: 0.786990786590909

00:36:56.067 --> 00:36:58.150 of things like NFL and GFAP.
NOTE Confidence: 0.786990786590909

00:36:58.150 --> 00:37:00.610 Ubiquitously in people who do not

NOTE Confidence: 0.786990786590909
00:37:00.610 --> 00:37:02.540 have any neurologic symptoms,
NOTE Confidence: 0.786990786590909
00:37:02.540 --> 00:37:04.238 and we haven't seen an avalanche
NOTE Confidence: 0.786990786590909
00:37:04.238 --> 00:37:05.799 of things of nerve degenerative
NOTE Confidence: 0.786990786590909
00:37:05.799 --> 00:37:07.634 disease such as Alzheimer's and
NOTE Confidence: 0.786990786590909
00:37:07.634 --> 00:37:09.880 people who've had HIV for 40 years,
NOTE Confidence: 0.786990786590909
00:37:09.880 --> 00:37:11.512 so I think what this means
NOTE Confidence: 0.786990786590909
00:37:11.512 --> 00:37:12.600 clinically is is unclear,
NOTE Confidence: 0.786990786590909
00:37:12.600 --> 00:37:14.592 but it does suggest that there's
NOTE Confidence: 0.786990786590909
00:37:14.592 --> 00:37:15.920 some neuronal injury during
NOTE Confidence: 0.786990786590909
00:37:15.983 --> 00:37:17.478 the time of acute COVID-19.
NOTE Confidence: 0.786990786590909
00:37:17.480 --> 00:37:20.048 So all of this leads to this sort
NOTE Confidence: 0.786990786590909
00:37:20.048 --> 00:37:22.500 of very oversimplified figure,
NOTE Confidence: 0.786990786590909
00:37:22.500 --> 00:37:24.124 which is actually a beautiful figure put
NOTE Confidence: 0.786990786590909
00:37:24.124 --> 00:37:27.340 together by the science illustrators.
NOTE Confidence: 0.786990786590909
00:37:27.340 --> 00:37:27.740 That summarizes,
NOTE Confidence: 0.786990786590909

00:37:27.740 --> 00:37:29.340 I think what I've told you so far,
NOTE Confidence: 0.786990786590909

00:37:29.340 --> 00:37:31.244 so we think in the upper left that
NOTE Confidence: 0.786990786590909

00:37:31.244 --> 00:37:32.771 there's really generalized inflammation
NOTE Confidence: 0.786990786590909

00:37:32.771 --> 00:37:34.775 and generalizing neural inflammation.
NOTE Confidence: 0.786990786590909

00:37:34.780 --> 00:37:36.108 Immune cells,
NOTE Confidence: 0.786990786590909

00:37:36.108 --> 00:37:39.060 including monocytes and CD8T cells and CD.
NOTE Confidence: 0.786990786590909

00:37:39.060 --> 00:37:39.540 Four cells,
NOTE Confidence: 0.786990786590909

00:37:39.540 --> 00:37:42.498 probably traffic into the nervous system.
NOTE Confidence: 0.786990786590909

00:37:42.500 --> 00:37:43.545 You don't necessarily have to
NOTE Confidence: 0.786990786590909

00:37:43.545 --> 00:37:44.932 have a broken down blood brain
NOTE Confidence: 0.786990786590909

00:37:44.932 --> 00:37:46.140 barrier for cellular trafficking,
NOTE Confidence: 0.786990786590909

00:37:46.140 --> 00:37:46.616 of course,
NOTE Confidence: 0.786990786590909

00:37:46.616 --> 00:37:48.282 but there may be some blood brain
NOTE Confidence: 0.786990786590909

00:37:48.282 --> 00:37:49.259 barrier injury as well,
NOTE Confidence: 0.786990786590909

00:37:49.260 --> 00:37:51.120 and then cytokines and antibodies
NOTE Confidence: 0.786990786590909

00:37:51.120 --> 00:37:53.724 also seem to be diffusing into the

NOTE Confidence: 0.786990786590909

00:37:53.724 --> 00:37:55.758 nervous system and into the brain.

NOTE Confidence: 0.786990786590909

00:37:55.760 --> 00:37:57.870 There is also antibody production.

NOTE Confidence: 0.786990786590909

00:37:57.870 --> 00:37:59.338 Which may be exacerbating

NOTE Confidence: 0.786990786590909

00:37:59.338 --> 00:38:00.439 the nerve inflammation,

NOTE Confidence: 0.786990786590909

00:38:00.440 --> 00:38:02.150 and there seems to be production

NOTE Confidence: 0.786990786590909

00:38:02.150 --> 00:38:03.610 of antibodies both to SARS,

NOTE Confidence: 0.786990786590909

00:38:03.610 --> 00:38:06.133 Co V2 that are entering the brain and

NOTE Confidence: 0.786990786590909

00:38:06.133 --> 00:38:07.548 persisting potentially in the brain,

NOTE Confidence: 0.786990786590909

00:38:07.550 --> 00:38:09.034 and then also autoantibodies.

NOTE Confidence: 0.786990786590909

00:38:09.034 --> 00:38:10.518 There's limited presence of

NOTE Confidence: 0.786990786590909

00:38:10.518 --> 00:38:12.501 the viral proteins or a viral

NOTE Confidence: 0.786990786590909

00:38:12.501 --> 00:38:14.265 particles in the neurons based on

NOTE Confidence: 0.786990786590909

00:38:14.323 --> 00:38:16.208 all the current detection methods,

NOTE Confidence: 0.786990786590909

00:38:16.210 --> 00:38:17.848 although you know more research has

NOTE Confidence: 0.786990786590909

00:38:17.848 --> 00:38:20.080 to be done and there seems to be at

NOTE Confidence: 0.786990786590909

00:38:20.080 --> 00:38:22.199 least some level of microvascular injury.

NOTE Confidence: 0.786990786590909

00:38:22.200 --> 00:38:23.844 Some of this may be related

NOTE Confidence: 0.786990786590909

00:38:23.844 --> 00:38:24.666 to endothelial injury,

NOTE Confidence: 0.786990786590909

00:38:24.670 --> 00:38:27.248 some of it's related to micro clotting.

NOTE Confidence: 0.786990786590909

00:38:27.248 --> 00:38:29.462 And some of this may also

NOTE Confidence: 0.786990786590909

00:38:29.462 --> 00:38:30.810 be underlying disease.

NOTE Confidence: 0.786990786590909

00:38:30.810 --> 00:38:32.784 Which of these mechanisms are primarily

NOTE Confidence: 0.786990786590909

00:38:32.784 --> 00:38:35.198 leading to the signs of neuronal injury?

NOTE Confidence: 0.786990786590909

00:38:35.200 --> 00:38:37.250 I think are not certain.

NOTE Confidence: 0.786990786590909

00:38:37.250 --> 00:38:38.834 But I think that it's important

NOTE Confidence: 0.786990786590909

00:38:38.834 --> 00:38:40.654 to think that there are also

NOTE Confidence: 0.786990786590909

00:38:40.654 --> 00:38:42.429 susceptibility factors such as genetic,

NOTE Confidence: 0.786990786590909

00:38:42.430 --> 00:38:43.502 pre-existing comorbidities,

NOTE Confidence: 0.786990786590909

00:38:43.502 --> 00:38:47.254 and immune status that may be contributing.

NOTE Confidence: 0.786990786590909

00:38:47.260 --> 00:38:49.618 So I'm gonna spend the rest

NOTE Confidence: 0.786990786590909

00:38:49.618 --> 00:38:52.239 of my talk really focused on.

NOTE Confidence: 0.786990786590909
00:38:52.240 --> 00:38:53.740 The mystery of long COVID,
NOTE Confidence: 0.786990786590909
00:38:53.740 --> 00:38:55.476 and I suspect that for most people,
NOTE Confidence: 0.786990786590909
00:38:55.480 --> 00:38:56.746 this is the part that they
NOTE Confidence: 0.786990786590909
00:38:56.746 --> 00:38:57.900 really have heard less about,
NOTE Confidence: 0.786990786590909
00:38:57.900 --> 00:38:59.860 and I'm I'm hoping that to show a
NOTE Confidence: 0.786990786590909
00:38:59.860 --> 00:39:01.748 little bit of light on this so very
NOTE Confidence: 0.786990786590909
00:39:01.748 --> 00:39:03.398 early on in the pandemic there's
NOTE Confidence: 0.786990786590909
00:39:03.398 --> 00:39:05.504 there was some kind of popular
NOTE Confidence: 0.786990786590909
00:39:05.504 --> 00:39:07.116 press reporting of people saying,
NOTE Confidence: 0.786990786590909
00:39:07.116 --> 00:39:07.720 you know,
NOTE Confidence: 0.786990786590909
00:39:07.720 --> 00:39:09.918 I really am having trouble with this
NOTE Confidence: 0.786990786590909
00:39:09.918 --> 00:39:11.868 feeling that I have dementia and
NOTE Confidence: 0.786990786590909
00:39:11.868 --> 00:39:14.066 this term brain fog has come out.
NOTE Confidence: 0.786990786590909
00:39:14.070 --> 00:39:15.850 There's also being more scientific
NOTE Confidence: 0.786990786590909
00:39:15.850 --> 00:39:17.630 reports talking about these issues,
NOTE Confidence: 0.899939165

00:39:17.630 --> 00:39:20.926 and now it's really emerged that there are
NOTE Confidence: 0.899939165

00:39:20.926 --> 00:39:23.607 persistent issues relating to mental health.
NOTE Confidence: 0.899939165

00:39:23.610 --> 00:39:26.082 Affective disorders psychiatric
NOTE Confidence: 0.899939165

00:39:26.082 --> 00:39:28.287 psychosis disorders, cardiovascular,
NOTE Confidence: 0.899939165

00:39:28.287 --> 00:39:31.629 etc that are really persisting after
NOTE Confidence: 0.899939165

00:39:31.629 --> 00:39:34.566 COVID-19 and so really what we have.
NOTE Confidence: 0.899939165

00:39:34.570 --> 00:39:37.261 What we have done is again as I mentioned
NOTE Confidence: 0.899939165

00:39:37.261 --> 00:39:39.983 for the first wave we initially have
NOTE Confidence: 0.899939165

00:39:39.983 --> 00:39:42.448 learned about this through a clinical
NOTE Confidence: 0.899939165

00:39:42.448 --> 00:39:44.920 response and along with a really
NOTE Confidence: 0.899939165

00:39:44.920 --> 00:39:46.688 fantastic partners associated with
NOTE Confidence: 0.899939165

00:39:46.688 --> 00:39:48.564 running this multidisciplinary COVID-19
NOTE Confidence: 0.899939165

00:39:48.564 --> 00:39:50.936 recovery clinic which is directed
NOTE Confidence: 0.899939165

00:39:50.936 --> 00:39:53.086 by Jennifer Plastics and pulmonary.
NOTE Confidence: 0.899939165

00:39:53.090 --> 00:39:55.578 And colleagues and psychiatry,
NOTE Confidence: 0.899939165

00:39:55.578 --> 00:39:58.688 Dr Klingensmith and Doctor Fisher.

NOTE Confidence: 0.899939165

00:39:58.690 --> 00:40:00.652 We have been involved in seeing

NOTE Confidence: 0.899939165

00:40:00.652 --> 00:40:02.420 people who have recovered from

NOTE Confidence: 0.899939165

00:40:02.420 --> 00:40:04.425 COVID-19 but have lingering symptoms,

NOTE Confidence: 0.899939165

00:40:04.430 --> 00:40:06.110 and by October 2020 it became

NOTE Confidence: 0.899939165

00:40:06.110 --> 00:40:08.266 clear that there was really a large

NOTE Confidence: 0.899939165

00:40:08.266 --> 00:40:10.216 demand for people who are having

NOTE Confidence: 0.899939165

00:40:10.216 --> 00:40:11.610 persistent neurologic issues,

NOTE Confidence: 0.899939165

00:40:11.610 --> 00:40:13.650 and so again with my wonderful

NOTE Confidence: 0.899939165

00:40:13.650 --> 00:40:15.010 fellow stone Lindsay Farhadian.

NOTE Confidence: 0.899939165

00:40:15.010 --> 00:40:17.845 I'm let Lindsey and McAlpine began

NOTE Confidence: 0.899939165

00:40:17.845 --> 00:40:19.855 to run this clinic that's focused

NOTE Confidence: 0.899939165

00:40:19.855 --> 00:40:22.082 on these disorders and what you can

NOTE Confidence: 0.899939165

00:40:22.082 --> 00:40:23.816 see here are the chief complaints

NOTE Confidence: 0.899939165

00:40:23.878 --> 00:40:26.065 of the people who the 1st 300 or so

NOTE Confidence: 0.899939165

00:40:26.065 --> 00:40:28.330 people who came into our clinic.

NOTE Confidence: 0.899939165

00:40:28.330 --> 00:40:29.802 Again, there's a separate.
NOTE Confidence: 0.899939165

00:40:29.802 --> 00:40:30.906 Psychiatry referral clinics.
NOTE Confidence: 0.899939165

00:40:30.910 --> 00:40:32.692 So we were not primarily seeing
NOTE Confidence: 0.899939165

00:40:32.692 --> 00:40:34.779 people who are having severe anxiety,
NOTE Confidence: 0.899939165

00:40:34.780 --> 00:40:36.226 depression, PTSD, psychosis.
NOTE Confidence: 0.899939165

00:40:36.226 --> 00:40:38.859 These kinds of things so you can
NOTE Confidence: 0.899939165

00:40:38.859 --> 00:40:40.584 see that 60% of these people are
NOTE Confidence: 0.899939165

00:40:40.584 --> 00:40:41.864 coming in with cognitive impairment,
NOTE Confidence: 0.899939165

00:40:41.870 --> 00:40:43.962 others with neuromuscular complaints
NOTE Confidence: 0.899939165

00:40:43.962 --> 00:40:45.008 and headache.
NOTE Confidence: 0.899939165

00:40:45.010 --> 00:40:46.570 And a few things have emerged
NOTE Confidence: 0.899939165

00:40:46.570 --> 00:40:47.610 that have been interesting.
NOTE Confidence: 0.899939165

00:40:47.610 --> 00:40:49.014 First of all, surprisingly,
NOTE Confidence: 0.899939165

00:40:49.014 --> 00:40:50.067 in the clinic,
NOTE Confidence: 0.899939165

00:40:50.070 --> 00:40:52.770 the median age is less than 50 years old.
NOTE Confidence: 0.899939165

00:40:52.770 --> 00:40:54.930 So rather than what we might have expected,

NOTE Confidence: 0.899939165

00:40:54.930 --> 00:40:57.142 which is people who would have the

NOTE Confidence: 0.899939165

00:40:57.142 --> 00:40:59.340 most severe course of acute COVID-19

NOTE Confidence: 0.899939165

00:40:59.340 --> 00:41:01.310 like being hospitalized had had

NOTE Confidence: 0.899939165

00:41:01.310 --> 00:41:03.165 prolonged severe illness related to

NOTE Confidence: 0.899939165

00:41:03.165 --> 00:41:05.169 their risk factors of being older

NOTE Confidence: 0.899939165

00:41:05.169 --> 00:41:07.420 and having a lot of comorbidities,

NOTE Confidence: 0.899939165

00:41:07.420 --> 00:41:09.516 we were actually seeing a lot of people

NOTE Confidence: 0.899939165

00:41:09.516 --> 00:41:11.330 who were young and the other really

NOTE Confidence: 0.899939165

00:41:11.330 --> 00:41:12.530 remarkable finding in this clinic,

NOTE Confidence: 0.899939165

00:41:12.530 --> 00:41:14.185 and this is completely echoing

NOTE Confidence: 0.899939165

00:41:14.185 --> 00:41:15.178 what's being found.

NOTE Confidence: 0.899939165

00:41:15.180 --> 00:41:17.646 Worldwide and people who are presenting

NOTE Confidence: 0.899939165

00:41:17.646 --> 00:41:19.830 lingering symptoms after COVID.

NOTE Confidence: 0.899939165

00:41:19.830 --> 00:41:21.447 Is that the vast majority of people

NOTE Confidence: 0.899939165

00:41:21.447 --> 00:41:23.057 who are coming into our clinic

NOTE Confidence: 0.899939165

00:41:23.057 --> 00:41:24.217 now with lingering symptoms,
NOTE Confidence: 0.899939165

00:41:24.220 --> 00:41:25.999 were never hospitalized.
NOTE Confidence: 0.899939165

00:41:25.999 --> 00:41:29.780 So while 19% did have ICU admission,
NOTE Confidence: 0.899939165

00:41:29.780 --> 00:41:33.130 67% of people completely convalesced at home,
NOTE Confidence: 0.899939165

00:41:33.130 --> 00:41:36.378 reflecting the fact that they had mild COVID.
NOTE Confidence: 0.899939165

00:41:36.380 --> 00:41:39.120 So what does that mean?
NOTE Confidence: 0.899939165

00:41:39.120 --> 00:41:40.160 What are some of the?
NOTE Confidence: 0.899939165

00:41:40.160 --> 00:41:41.959 What are some of the stories that
NOTE Confidence: 0.899939165

00:41:41.959 --> 00:41:43.310 we had with patients?
NOTE Confidence: 0.899939165

00:41:43.310 --> 00:41:45.776 Well, here are just some examples.
NOTE Confidence: 0.899939165

00:41:45.780 --> 00:41:47.341 So one of the types of syndromes
NOTE Confidence: 0.899939165

00:41:47.341 --> 00:41:48.952 that we've seen are people who
NOTE Confidence: 0.899939165

00:41:48.952 --> 00:41:50.144 are having cognitive problems,
NOTE Confidence: 0.899939165

00:41:50.150 --> 00:41:53.238 and this is an example of a patient.
NOTE Confidence: 0.899939165

00:41:53.240 --> 00:41:55.712 They they presented to us saying that they
NOTE Confidence: 0.899939165

00:41:55.712 --> 00:41:57.879 were having trouble remembering tasks,

NOTE Confidence: 0.899939165

00:41:57.880 --> 00:41:59.664 conversations needing a notepad

NOTE Confidence: 0.899939165

00:41:59.664 --> 00:42:02.340 to write things down during calls,

NOTE Confidence: 0.899939165

00:42:02.340 --> 00:42:03.488 writing emails and correspondence,

NOTE Confidence: 0.899939165

00:42:03.488 --> 00:42:05.900 taking two to three times as long as usual,

NOTE Confidence: 0.899939165

00:42:05.900 --> 00:42:07.216 and one of the things that brought

NOTE Confidence: 0.899939165

00:42:07.216 --> 00:42:08.100 them into our clinic.

NOTE Confidence: 0.899939165

00:42:08.100 --> 00:42:09.666 Finally is that they were unable

NOTE Confidence: 0.899939165

00:42:09.666 --> 00:42:11.480 to follow a recipe to bake bread,

NOTE Confidence: 0.899939165

00:42:11.480 --> 00:42:13.736 and this is a physician who of course

NOTE Confidence: 0.899939165

00:42:13.736 --> 00:42:16.137 you know all of these things would

NOTE Confidence: 0.899939165

00:42:16.137 --> 00:42:17.912 be second nature and unthinkable

NOTE Confidence: 0.824273793181818

00:42:17.980 --> 00:42:19.896 before COVID-19 another patient reflected

NOTE Confidence: 0.824273793181818

00:42:19.896 --> 00:42:21.888 sort of another category of people

NOTE Confidence: 0.824273793181818

00:42:21.888 --> 00:42:23.860 that we're seeing which is headache.

NOTE Confidence: 0.824273793181818

00:42:23.860 --> 00:42:25.796 And for some people this has been happening

NOTE Confidence: 0.824273793181818

00:42:25.796 --> 00:42:27.569 in people who had severe headache as
NOTE Confidence: 0.824273793181818

00:42:27.569 --> 00:42:29.220 part of their initial COVID illness.
NOTE Confidence: 0.824273793181818

00:42:29.220 --> 00:42:32.363 But headaches then lasting daily for months
NOTE Confidence: 0.824273793181818

00:42:32.363 --> 00:42:35.647 and months and fearing with their jobs.
NOTE Confidence: 0.824273793181818

00:42:35.650 --> 00:42:38.370 We've also had numbers of people who are
NOTE Confidence: 0.824273793181818

00:42:38.370 --> 00:42:40.509 having patchy sensory abnormalities,
NOTE Confidence: 0.824273793181818

00:42:40.510 --> 00:42:41.788 and this is something that unfortunately,
NOTE Confidence: 0.824273793181818

00:42:41.790 --> 00:42:43.006 we're continuing to see.
NOTE Confidence: 0.824273793181818

00:42:43.006 --> 00:42:46.150 We just have a patient who had a breakthrough
NOTE Confidence: 0.824273793181818

00:42:46.150 --> 00:42:48.240 infection of Omicron after complete
NOTE Confidence: 0.824273793181818

00:42:48.240 --> 00:42:50.456 vaccination and booster who's having
NOTE Confidence: 0.824273793181818

00:42:50.456 --> 00:42:52.656 patchy sensory changes after COVID-19.
NOTE Confidence: 0.824273793181818

00:42:52.660 --> 00:42:53.260 And finally,
NOTE Confidence: 0.824273793181818

00:42:53.260 --> 00:42:55.660 this is a case that's well known to
NOTE Confidence: 0.824273793181818

00:42:55.727 --> 00:42:57.863 many people in psychiatry because we
NOTE Confidence: 0.824273793181818

00:42:57.863 --> 00:43:00.170 share taking care of this patient.

NOTE Confidence: 0.824273793181818

00:43:00.170 --> 00:43:01.850 People such as this gentleman a 30

NOTE Confidence: 0.824273793181818

00:43:01.850 --> 00:43:04.057 year old man with no past psychiatric

NOTE Confidence: 0.824273793181818

00:43:04.057 --> 00:43:05.489 history who developed paranoia,

NOTE Confidence: 0.824273793181818

00:43:05.490 --> 00:43:05.839 delusions,

NOTE Confidence: 0.824273793181818

00:43:05.839 --> 00:43:08.282 hypersomnolence in a few weeks after COVID-19

NOTE Confidence: 0.824273793181818

00:43:08.282 --> 00:43:10.650 that was refractory to anti psychotics.

NOTE Confidence: 0.824273793181818

00:43:10.650 --> 00:43:12.562 So these are some of the sort of

NOTE Confidence: 0.824273793181818

00:43:12.562 --> 00:43:13.708 individual stories and I'll tell

NOTE Confidence: 0.824273793181818

00:43:13.708 --> 00:43:15.478 you that the more and more you hear

NOTE Confidence: 0.824273793181818

00:43:15.478 --> 00:43:17.410 from people around the world who are

NOTE Confidence: 0.824273793181818

00:43:17.410 --> 00:43:19.110 experiencing lung COVID the more and

NOTE Confidence: 0.824273793181818

00:43:19.110 --> 00:43:21.245 more you hear stories that are very

NOTE Confidence: 0.824273793181818

00:43:21.245 --> 00:43:23.435 very similar to these individual tales.

NOTE Confidence: 0.824273793181818

00:43:23.440 --> 00:43:25.904 So what do we know from research standpoint

NOTE Confidence: 0.824273793181818

00:43:25.904 --> 00:43:28.130 about this condition about long COVID,

NOTE Confidence: 0.824273793181818

00:43:28.130 --> 00:43:29.754 though some of the best data has
NOTE Confidence: 0.824273793181818

00:43:29.754 --> 00:43:31.140 actually come from the community,
NOTE Confidence: 0.824273793181818

00:43:31.140 --> 00:43:33.275 and this has really been a remarkable
NOTE Confidence: 0.824273793181818

00:43:33.275 --> 00:43:35.899 effort from a group called the patient
NOTE Confidence: 0.824273793181818

00:43:35.899 --> 00:43:37.959 LED Resource Consortium for COVID-19.
NOTE Confidence: 0.824273793181818

00:43:37.960 --> 00:43:41.061 Some of the people in this consortium
NOTE Confidence: 0.824273793181818

00:43:41.061 --> 00:43:43.200 are actually neuroscientists originally,
NOTE Confidence: 0.824273793181818

00:43:43.200 --> 00:43:45.288 many people or people who have
NOTE Confidence: 0.824273793181818

00:43:45.288 --> 00:43:47.060 been in researching other ways.
NOTE Confidence: 0.824273793181818

00:43:47.060 --> 00:43:48.620 But once they experienced kovid and
NOTE Confidence: 0.824273793181818

00:43:48.620 --> 00:43:50.551 then had a what they called long
NOTE Confidence: 0.824273793181818

00:43:50.551 --> 00:43:52.231 COVID symptoms and the term long
NOTE Confidence: 0.824273793181818

00:43:52.231 --> 00:43:53.836 COVID has really come from the.
NOTE Confidence: 0.824273793181818

00:43:53.840 --> 00:43:55.500 Community,
NOTE Confidence: 0.824273793181818

00:43:55.500 --> 00:43:57.216 they have really come forward to
NOTE Confidence: 0.824273793181818

00:43:57.216 --> 00:43:59.530 try to be advocates and involved in

NOTE Confidence: 0.824273793181818
00:43:59.530 --> 00:44:01.385 research and setting research agendas,
NOTE Confidence: 0.824273793181818
00:44:01.390 --> 00:44:04.100 so this is a study that has a lot of caveats.
NOTE Confidence: 0.824273793181818
00:44:04.100 --> 00:44:05.000 Online survey.
NOTE Confidence: 0.824273793181818
00:44:05.000 --> 00:44:06.800 Not everyone was documented
NOTE Confidence: 0.824273793181818
00:44:06.800 --> 00:44:08.600 to actually have COVID,
NOTE Confidence: 0.824273793181818
00:44:08.600 --> 00:44:10.880 but it is a survey that I think
NOTE Confidence: 0.824273793181818
00:44:10.880 --> 00:44:12.618 reflects what the current knowledge
NOTE Confidence: 0.824273793181818
00:44:12.618 --> 00:44:14.814 is of us long COVID worldwide.
NOTE Confidence: 0.824273793181818
00:44:14.820 --> 00:44:16.696 So this is something that revealed a
NOTE Confidence: 0.824273793181818
00:44:16.696 --> 00:44:18.519 couple of really important messages.
NOTE Confidence: 0.824273793181818
00:44:18.520 --> 00:44:19.564 First of all,
NOTE Confidence: 0.824273793181818
00:44:19.564 --> 00:44:21.304 this is people reporting their
NOTE Confidence: 0.824273793181818
00:44:21.304 --> 00:44:23.142 average number of symptoms over
NOTE Confidence: 0.824273793181818
00:44:23.142 --> 00:44:24.947 seven months after having COVID.
NOTE Confidence: 0.824273793181818
00:44:24.950 --> 00:44:26.910 And what you can see here is that
NOTE Confidence: 0.824273793181818

00:44:26.910 --> 00:44:28.883 while many many people have recovery
NOTE Confidence: 0.824273793181818

00:44:28.883 --> 00:44:30.663 overtime with gradual decrement in
NOTE Confidence: 0.824273793181818

00:44:30.663 --> 00:44:32.807 the number of symptoms over months,
NOTE Confidence: 0.824273793181818

00:44:32.810 --> 00:44:35.386 there's a large number of people in
NOTE Confidence: 0.824273793181818

00:44:35.386 --> 00:44:37.950 this reported study that actually had
NOTE Confidence: 0.824273793181818

00:44:37.950 --> 00:44:40.260 frequent and numerous symptoms lasting
NOTE Confidence: 0.824273793181818

00:44:40.260 --> 00:44:42.997 seven months and longer after COVID-19.
NOTE Confidence: 0.824273793181818

00:44:43.000 --> 00:44:44.130 And what really came out
NOTE Confidence: 0.824273793181818

00:44:44.130 --> 00:44:45.034 in this initial report,
NOTE Confidence: 0.824273793181818

00:44:45.040 --> 00:44:47.455 which I think is really extremely important,
NOTE Confidence: 0.824273793181818

00:44:47.460 --> 00:44:48.504 is that many,
NOTE Confidence: 0.824273793181818

00:44:48.504 --> 00:44:50.592 many of the symptoms people are
NOTE Confidence: 0.824273793181818

00:44:50.592 --> 00:44:52.740 having are considered what they
NOTE Confidence: 0.824273793181818

00:44:52.740 --> 00:44:54.900 consider to be neuro psychiatric.
NOTE Confidence: 0.824273793181818

00:44:54.900 --> 00:44:57.267 So you can see at the top what they
NOTE Confidence: 0.824273793181818

00:44:57.267 --> 00:44:59.408 call brain fog, memory issues,

NOTE Confidence: 0.824273793181818
00:44:59.408 --> 00:45:02.278 sensory changes in the middle,
NOTE Confidence: 0.824273793181818
00:45:02.280 --> 00:45:05.118 and then what they call headache
NOTE Confidence: 0.824273793181818
00:45:05.118 --> 00:45:06.064 and insomnia.
NOTE Confidence: 0.824273793181818
00:45:06.070 --> 00:45:07.915 Being major features of some
NOTE Confidence: 0.824273793181818
00:45:07.915 --> 00:45:09.760 of these most lasting symptoms
NOTE Confidence: 0.874153357368421
00:45:09.832 --> 00:45:11.962 after COVID and I think has
NOTE Confidence: 0.874153357368421
00:45:11.962 --> 00:45:13.027 really drawn attention.
NOTE Confidence: 0.874153357368421
00:45:13.030 --> 00:45:15.564 And what is a is an incredibly
NOTE Confidence: 0.874153357368421
00:45:15.564 --> 00:45:17.070 important problem for many,
NOTE Confidence: 0.874153357368421
00:45:17.070 --> 00:45:18.710 many people worldwide and trying
NOTE Confidence: 0.874153357368421
00:45:18.710 --> 00:45:20.813 to understand what may be the
NOTE Confidence: 0.874153357368421
00:45:20.813 --> 00:45:21.970 ideologies that challenges.
NOTE Confidence: 0.874153357368421
00:45:21.970 --> 00:45:23.870 There's really been very little
NOTE Confidence: 0.874153357368421
00:45:23.870 --> 00:45:25.375 systematic research into the
NOTE Confidence: 0.874153357368421
00:45:25.375 --> 00:45:27.247 ideologies of these conditions so far.
NOTE Confidence: 0.874153357368421

00:45:27.250 --> 00:45:28.990 There's major research efforts worldwide,
NOTE Confidence: 0.874153357368421

00:45:28.990 --> 00:45:30.866 of course, so this is a study
NOTE Confidence: 0.874153357368421

00:45:30.866 --> 00:45:32.450 that's a little interesting.
NOTE Confidence: 0.874153357368421

00:45:32.450 --> 00:45:35.422 It's a study that came out a few months ago,
NOTE Confidence: 0.874153357368421

00:45:35.422 --> 00:45:37.180 and there's actually been a follow-up
NOTE Confidence: 0.874153357368421

00:45:37.237 --> 00:45:39.182 PET study really finding similar
NOTE Confidence: 0.874153357368421

00:45:39.182 --> 00:45:41.127 findings by another group independently.
NOTE Confidence: 0.874153357368421

00:45:41.130 --> 00:45:43.686 This is a group that looked at 45 people.
NOTE Confidence: 0.874153357368421

00:45:43.690 --> 00:45:45.818 Had persistent cognitive symptoms
NOTE Confidence: 0.874153357368421

00:45:45.818 --> 00:45:48.478 or psychiatric symptoms and median
NOTE Confidence: 0.874153357368421

00:45:48.478 --> 00:45:51.469 of three months after COVID-19 and
NOTE Confidence: 0.874153357368421

00:45:51.469 --> 00:45:53.623 what they found was that there
NOTE Confidence: 0.874153357368421

00:45:53.623 --> 00:45:54.700 was regional hypometabolism.
NOTE Confidence: 0.874153357368421

00:45:54.700 --> 00:45:56.704 Looking at FDG pet compared to
NOTE Confidence: 0.874153357368421

00:45:56.704 --> 00:45:58.428 pretty well matched healthy controls
NOTE Confidence: 0.874153357368421

00:45:58.428 --> 00:46:00.396 and what was interesting in this

NOTE Confidence: 0.874153357368421
00:46:00.396 --> 00:46:02.634 finding is that the metabolic values
NOTE Confidence: 0.874153357368421
00:46:02.634 --> 00:46:04.222 actually associated with symptoms
NOTE Confidence: 0.874153357368421
00:46:04.222 --> 00:46:06.320 in this fairly small study,
NOTE Confidence: 0.874153357368421
00:46:06.320 --> 00:46:07.670 we don't know,
NOTE Confidence: 0.874153357368421
00:46:07.670 --> 00:46:08.350 of course,
NOTE Confidence: 0.874153357368421
00:46:08.350 --> 00:46:10.390 is whether some of these regional
NOTE Confidence: 0.874153357368421
00:46:10.390 --> 00:46:11.977 hypometabolism I'm from metabolism
NOTE Confidence: 0.874153357368421
00:46:11.977 --> 00:46:13.252 differences were actually
NOTE Confidence: 0.874153357368421
00:46:13.252 --> 00:46:14.527 present before COVID.
NOTE Confidence: 0.874153357368421
00:46:14.530 --> 00:46:16.810 And whether they were somehow people
NOTE Confidence: 0.874153357368421
00:46:16.810 --> 00:46:19.100 who were sensitive to having some
NOTE Confidence: 0.874153357368421
00:46:19.100 --> 00:46:21.356 of these syndromes after COVID so
NOTE Confidence: 0.874153357368421
00:46:21.356 --> 00:46:23.312 a really beautiful study that was
NOTE Confidence: 0.874153357368421
00:46:23.312 --> 00:46:24.673 actually just officially published
NOTE Confidence: 0.874153357368421
00:46:24.673 --> 00:46:26.599 last week that was actually reported
NOTE Confidence: 0.874153357368421

00:46:26.599 --> 00:46:28.756 as a preprint last summer gets around
NOTE Confidence: 0.874153357368421

00:46:28.756 --> 00:46:30.940 a little bit of that issue so this
NOTE Confidence: 0.874153357368421

00:46:31.006 --> 00:46:33.463 is a study that takes advantage of
NOTE Confidence: 0.874153357368421

00:46:33.463 --> 00:46:34.903 the absolutely fantastic resource
NOTE Confidence: 0.874153357368421

00:46:34.903 --> 00:46:36.538 of the UK biobank study.
NOTE Confidence: 0.874153357368421

00:46:36.540 --> 00:46:38.610 Many of you may know about UK biobank study.
NOTE Confidence: 0.874153357368421

00:46:38.610 --> 00:46:41.646 It's basically a long term surveillance
NOTE Confidence: 0.874153357368421

00:46:41.646 --> 00:46:43.860 population based study that collects.
NOTE Confidence: 0.874153357368421

00:46:43.860 --> 00:46:46.275 All sorts of samples and data from
NOTE Confidence: 0.874153357368421

00:46:46.275 --> 00:46:47.901 thousands of people throughout the
NOTE Confidence: 0.874153357368421

00:46:47.901 --> 00:46:50.492 UK over years and it's this has been
NOTE Confidence: 0.874153357368421

00:46:50.492 --> 00:46:52.247 an amazing resource for studying,
NOTE Confidence: 0.874153357368421

00:46:52.250 --> 00:46:52.954 for example,
NOTE Confidence: 0.874153357368421

00:46:52.954 --> 00:46:54.714 genetic diseases and rare disorders,
NOTE Confidence: 0.874153357368421

00:46:54.720 --> 00:46:56.200 and they collect things like
NOTE Confidence: 0.874153357368421

00:46:56.200 --> 00:46:58.160 echoes in a subset of people.

NOTE Confidence: 0.874153357368421

00:46:58.160 --> 00:47:00.170 They collect all sorts of blood

NOTE Confidence: 0.874153357368421

00:47:00.170 --> 00:47:02.725 and CSF and other data and other

NOTE Confidence: 0.874153357368421

00:47:02.725 --> 00:47:05.155 people limited neuro psych data in

NOTE Confidence: 0.874153357368421

00:47:05.155 --> 00:47:07.782 all of the participants and then

NOTE Confidence: 0.874153357368421

00:47:07.782 --> 00:47:09.487 in some subsets of participants

NOTE Confidence: 0.874153357368421

00:47:09.487 --> 00:47:11.319 they do serial MRI imaging.

NOTE Confidence: 0.874153357368421

00:47:11.320 --> 00:47:12.608 And so this is a wonderful study,

NOTE Confidence: 0.874153357368421

00:47:12.610 --> 00:47:14.146 but didn't manage of the fact

NOTE Confidence: 0.874153357368421

00:47:14.146 --> 00:47:15.474 that they identified that they

NOTE Confidence: 0.874153357368421

00:47:15.474 --> 00:47:16.719 had participants in the UK.

NOTE Confidence: 0.874153357368421

00:47:16.720 --> 00:47:19.975 Biobank study that had SARS Co V2

NOTE Confidence: 0.874153357368421

00:47:19.975 --> 00:47:22.460 positive tests between their prior

NOTE Confidence: 0.874153357368421

00:47:22.460 --> 00:47:24.955 scan in their usual surveillance

NOTE Confidence: 0.874153357368421

00:47:24.955 --> 00:47:27.784 system and then their follow up

NOTE Confidence: 0.874153357368421

00:47:27.784 --> 00:47:30.167 scan and they were able to do a

NOTE Confidence: 0.874153357368421

00:47:30.167 --> 00:47:31.716 really really deep chart analysis
NOTE Confidence: 0.874153357368421

00:47:31.716 --> 00:47:34.268 to identify what I think is a fairly
NOTE Confidence: 0.874153357368421

00:47:34.331 --> 00:47:36.086 convincing group of 384 controls
NOTE Confidence: 0.874153357368421

00:47:36.086 --> 00:47:38.350 that really do not seem to have had
NOTE Confidence: 0.874153357368421

00:47:38.417 --> 00:47:40.734 COVID based on lab tests and other
NOTE Confidence: 0.874153357368421

00:47:40.734 --> 00:47:42.320 data that's available in there.
NOTE Confidence: 0.874153357368421

00:47:42.320 --> 00:47:44.609 Charts which can be linked to the
NOTE Confidence: 0.874153357368421

00:47:44.609 --> 00:47:46.460 UK Biobank database and when they
NOTE Confidence: 0.874153357368421

00:47:46.460 --> 00:47:48.200 did this comparison and these people
NOTE Confidence: 0.874153357368421

00:47:48.200 --> 00:47:50.411 were also very well matched in terms
NOTE Confidence: 0.874153357368421

00:47:50.411 --> 00:47:52.449 intervals between scans and other factors.
NOTE Confidence: 0.874153357368421

00:47:52.450 --> 00:47:54.452 They found focal loss of Gray matter
NOTE Confidence: 0.874153357368421

00:47:54.452 --> 00:47:56.781 in a variety of brain structures in
NOTE Confidence: 0.874153357368421

00:47:56.781 --> 00:47:58.887 those people who would have COVID-19.
NOTE Confidence: 0.874153357368421

00:47:58.890 --> 00:48:01.594 Now the Gray matter loss was very small
NOTE Confidence: 0.874153357368421

00:48:01.594 --> 00:48:04.440 and and relative to Gray matter loss.

NOTE Confidence: 0.874153357368421

00:48:04.440 --> 00:48:06.090 All of the groups lost Gray

NOTE Confidence: 0.874153357368421

00:48:06.090 --> 00:48:07.190 matter over the two

NOTE Confidence: 0.85115896

00:48:07.258 --> 00:48:08.576 years. Both the healthy

NOTE Confidence: 0.85115896

00:48:08.576 --> 00:48:10.186 controls and the COVID group,

NOTE Confidence: 0.85115896

00:48:10.190 --> 00:48:12.774 but the COVID group lost more Gray matter.

NOTE Confidence: 0.85115896

00:48:12.780 --> 00:48:13.536 Maybe certain regions

NOTE Confidence: 0.85115896

00:48:13.536 --> 00:48:14.796 than the other group did.

NOTE Confidence: 0.85115896

00:48:14.800 --> 00:48:16.560 There were also some disruptions

NOTE Confidence: 0.85115896

00:48:16.560 --> 00:48:17.968 in DTI imaging metrics,

NOTE Confidence: 0.85115896

00:48:17.970 --> 00:48:20.400 suggesting some other structural changes.

NOTE Confidence: 0.85115896

00:48:20.400 --> 00:48:21.456 So what does this tell us?

NOTE Confidence: 0.85115896

00:48:21.460 --> 00:48:23.196 This is not an all time low on COVID.

NOTE Confidence: 0.85115896

00:48:23.200 --> 00:48:25.512 We have no idea whether any of these

NOTE Confidence: 0.85115896

00:48:25.512 --> 00:48:27.310 patients have long COVID symptoms.

NOTE Confidence: 0.85115896

00:48:27.310 --> 00:48:28.834 There were some changes in Neuro

NOTE Confidence: 0.85115896

00:48:28.834 --> 00:48:30.381 Psych testing overtime in the COVID
NOTE Confidence: 0.85115896

00:48:30.381 --> 00:48:31.827 group compared to the other group,
NOTE Confidence: 0.85115896

00:48:31.830 --> 00:48:33.370 and it wasn't convincingly shown
NOTE Confidence: 0.85115896

00:48:33.370 --> 00:48:34.910 to be associated with these
NOTE Confidence: 0.85115896

00:48:34.970 --> 00:48:36.358 changes in brain structure.
NOTE Confidence: 0.85115896

00:48:36.360 --> 00:48:38.096 But I think what this is really
NOTE Confidence: 0.85115896

00:48:38.096 --> 00:48:39.890 useful to tell us is there is
NOTE Confidence: 0.85115896

00:48:39.890 --> 00:48:41.378 a footprint of COVID effects in
NOTE Confidence: 0.85115896

00:48:41.436 --> 00:48:43.110 the brain that can be measured,
NOTE Confidence: 0.85115896

00:48:43.110 --> 00:48:44.772 which maybe gives us some more
NOTE Confidence: 0.85115896

00:48:44.772 --> 00:48:46.442 targets and even more sort of
NOTE Confidence: 0.85115896

00:48:46.442 --> 00:48:47.948 galvanizes us even more to try
NOTE Confidence: 0.85115896

00:48:47.948 --> 00:48:49.547 to study this question with the
NOTE Confidence: 0.85115896

00:48:49.547 --> 00:48:52.350 kinds of tools that we can use that
NOTE Confidence: 0.85115896

00:48:52.350 --> 00:48:54.810 we've developed for neuroscience.
NOTE Confidence: 0.85115896

00:48:54.810 --> 00:48:55.710 I'll say that there are,

NOTE Confidence: 0.85115896
00:48:55.710 --> 00:48:56.206 you know,
NOTE Confidence: 0.85115896
00:48:56.206 --> 00:48:57.942 one hypothesis might be that long COVID
NOTE Confidence: 0.85115896
00:48:57.942 --> 00:48:59.447 is associated with neuroinflammation and
NOTE Confidence: 0.85115896
00:48:59.447 --> 00:49:02.210 this is being sort of put out by many people,
NOTE Confidence: 0.85115896
00:49:02.210 --> 00:49:03.098 including our groups.
NOTE Confidence: 0.85115896
00:49:03.098 --> 00:49:04.578 We don't have really any
NOTE Confidence: 0.85115896
00:49:04.578 --> 00:49:05.650 convincing data for that.
NOTE Confidence: 0.85115896
00:49:05.650 --> 00:49:07.698 This is a tiny study that looked at
NOTE Confidence: 0.85115896
00:49:07.698 --> 00:49:09.470 some patients with cancer and World
NOTE Confidence: 0.85115896
00:49:09.470 --> 00:49:11.282 Sloan Kettering and looked at people
NOTE Confidence: 0.85115896
00:49:11.344 --> 00:49:12.934 who had cancer and neurological
NOTE Confidence: 0.85115896
00:49:12.934 --> 00:49:14.524 symptoms after COVID that are
NOTE Confidence: 0.85115896
00:49:14.530 --> 00:49:16.616 shown in the red and then looked
NOTE Confidence: 0.85115896
00:49:16.616 --> 00:49:18.354 at other comparison patients who
NOTE Confidence: 0.85115896
00:49:18.354 --> 00:49:20.319 had cancer and neurologic symptoms.
NOTE Confidence: 0.85115896

00:49:20.320 --> 00:49:22.150 But no kovid and found some
NOTE Confidence: 0.85115896

00:49:22.150 --> 00:49:23.851 higher levels of CSF inflammatory
NOTE Confidence: 0.85115896

00:49:23.851 --> 00:49:26.305 markers and those who had COVID.
NOTE Confidence: 0.85115896

00:49:26.310 --> 00:49:26.544 Much,
NOTE Confidence: 0.85115896

00:49:26.544 --> 00:49:28.182 much lower than those people who were
NOTE Confidence: 0.85115896

00:49:28.182 --> 00:49:29.580 treated with CAR T cell therapies,
NOTE Confidence: 0.85115896

00:49:29.580 --> 00:49:31.460 so I think it's hard to know really
NOTE Confidence: 0.85115896

00:49:31.460 --> 00:49:32.918 how clinically significant this is,
NOTE Confidence: 0.85115896

00:49:32.920 --> 00:49:35.209 but it's a hint that looking for
NOTE Confidence: 0.85115896

00:49:35.209 --> 00:49:37.040 neuroinflammation after Kovac may be helpful.
NOTE Confidence: 0.85115896

00:49:37.040 --> 00:49:39.300 Another group has looked prospectively
NOTE Confidence: 0.85115896

00:49:39.300 --> 00:49:42.117 and individuals who had acute COVID-19
NOTE Confidence: 0.85115896

00:49:42.117 --> 00:49:44.057 during hospitalization and then
NOTE Confidence: 0.85115896

00:49:44.057 --> 00:49:46.482 were followed over three months,
NOTE Confidence: 0.85115896

00:49:46.490 --> 00:49:47.790 and in this group,
NOTE Confidence: 0.85115896

00:49:47.790 --> 00:49:49.740 those people who had higher measures

NOTE Confidence: 0.85115896

00:49:49.807 --> 00:49:51.702 of depression and neurocognition 3

NOTE Confidence: 0.85115896

00:49:51.702 --> 00:49:54.130 months after COVID had higher baseline

NOTE Confidence: 0.85115896

00:49:54.130 --> 00:49:56.495 measures of blood inflammatory markers.

NOTE Confidence: 0.85115896

00:49:56.500 --> 00:49:58.505 Again suggesting that maybe an

NOTE Confidence: 0.85115896

00:49:58.505 --> 00:50:00.109 inflammatory hit could have

NOTE Confidence: 0.85115896

00:50:00.109 --> 00:50:01.949 resulted in more outcomes later,

NOTE Confidence: 0.85115896

00:50:01.950 --> 00:50:03.462 but of course there's lots of

NOTE Confidence: 0.85115896

00:50:03.462 --> 00:50:05.136 caveats for this kind of study and

NOTE Confidence: 0.85115896

00:50:05.136 --> 00:50:06.936 one issue I think for all of these

NOTE Confidence: 0.85115896

00:50:06.936 --> 00:50:08.898 studies that are based in primarily

NOTE Confidence: 0.85115896

00:50:08.898 --> 00:50:10.502 hospitalized patients is that it's

NOTE Confidence: 0.85115896

00:50:10.502 --> 00:50:12.368 really uncertain to know how these

NOTE Confidence: 0.85115896

00:50:12.368 --> 00:50:14.225 results to people who have milder

NOTE Confidence: 0.85115896

00:50:14.225 --> 00:50:16.840 forms of coverage or in their acute illness.

NOTE Confidence: 0.85115896

00:50:16.840 --> 00:50:19.400 And how they relate to longer term symptoms.

NOTE Confidence: 0.85115896

00:50:19.400 --> 00:50:20.327 So I mean,
NOTE Confidence: 0.85115896
00:50:20.327 --> 00:50:22.970 and by talking about the COVID mine study.
NOTE Confidence: 0.85115896
00:50:22.970 --> 00:50:23.666 And again,
NOTE Confidence: 0.85115896
00:50:23.666 --> 00:50:26.102 this is just really a preliminary study
NOTE Confidence: 0.85115896
00:50:26.102 --> 00:50:28.929 that we started over the last year at Yale.
NOTE Confidence: 0.85115896
00:50:28.930 --> 00:50:31.260 This is in collaboration with
NOTE Confidence: 0.85115896
00:50:31.260 --> 00:50:33.124 Shelly Farhadian against stellar
NOTE Confidence: 0.85115896
00:50:33.124 --> 00:50:35.376 physician investigator here and in
NOTE Confidence: 0.85115896
00:50:35.376 --> 00:50:37.156 new infectious disease and neurology,
NOTE Confidence: 0.85115896
00:50:37.160 --> 00:50:37.811 and an ID.
NOTE Confidence: 0.85115896
00:50:37.811 --> 00:50:39.330 And this is a study that's using
NOTE Confidence: 0.85115896
00:50:39.381 --> 00:50:41.117 a lot of the types of tools that
NOTE Confidence: 0.85115896
00:50:41.117 --> 00:50:43.037 we've been using over the years to
NOTE Confidence: 0.85115896
00:50:43.037 --> 00:50:44.472 look for subtle abnormalities and
NOTE Confidence: 0.7937471722222222
00:50:44.480 --> 00:50:46.630 people with acute HIV and
NOTE Confidence: 0.7937471722222222
00:50:46.630 --> 00:50:48.350 long term treated HIV.

NOTE Confidence: 0.793747172222222

00:50:48.350 --> 00:50:50.220 And essentially using these same

NOTE Confidence: 0.793747172222222

00:50:50.220 --> 00:50:52.090 really sense of interrogations to

NOTE Confidence: 0.793747172222222

00:50:52.147 --> 00:50:54.366 look for changes in people who are

NOTE Confidence: 0.793747172222222

00:50:54.366 --> 00:50:55.779 having neurologic and psychiatric

NOTE Confidence: 0.793747172222222

00:50:55.779 --> 00:50:57.387 complications months after COVID

NOTE Confidence: 0.793747172222222

00:50:57.387 --> 00:50:59.792 and most of these patients are

NOTE Confidence: 0.793747172222222

00:50:59.792 --> 00:51:02.144 referred from our neural COVID clinic

NOTE Confidence: 0.793747172222222

00:51:02.150 --> 00:51:03.970 and we really try to screen them

NOTE Confidence: 0.793747172222222

00:51:03.970 --> 00:51:05.837 to identify people who are having

NOTE Confidence: 0.793747172222222

00:51:05.837 --> 00:51:07.209 central nervous system symptoms,

NOTE Confidence: 0.793747172222222

00:51:07.210 --> 00:51:08.680 primarily because those are the

NOTE Confidence: 0.793747172222222

00:51:08.680 --> 00:51:10.350 kinds of tools we're focusing on,

NOTE Confidence: 0.793747172222222

00:51:10.350 --> 00:51:12.382 so you can see that we're using MRI

NOTE Confidence: 0.793747172222222

00:51:12.382 --> 00:51:14.360 brain really kind of detailed neuro

NOTE Confidence: 0.793747172222222

00:51:14.360 --> 00:51:16.484 psychiatric batteries of cognition and mood,

NOTE Confidence: 0.793747172222222

00:51:16.490 --> 00:51:17.970 lots of histories and surveys,
NOTE Confidence: 0.7937471722222222

00:51:17.970 --> 00:51:19.460 lots of information about their.
NOTE Confidence: 0.7937471722222222

00:51:19.460 --> 00:51:21.760 Acute illness and their ongoing
NOTE Confidence: 0.7937471722222222

00:51:21.760 --> 00:51:24.400 conditions and then doing very detailed
NOTE Confidence: 0.7937471722222222

00:51:24.400 --> 00:51:27.888 blood and CSF studies that range from
NOTE Confidence: 0.7937471722222222

00:51:27.888 --> 00:51:29.920 everywhere between immune profiling
NOTE Confidence: 0.7937471722222222

00:51:30.003 --> 00:51:32.213 with through single cell studies
NOTE Confidence: 0.7937471722222222

00:51:32.213 --> 00:51:34.488 to unique studies of antibodies,
NOTE Confidence: 0.7937471722222222

00:51:34.488 --> 00:51:36.316 autoantibodies and really high
NOTE Confidence: 0.7937471722222222

00:51:36.316 --> 00:51:38.220 level markers are looking for
NOTE Confidence: 0.7937471722222222

00:51:38.220 --> 00:51:39.476 evidence of viral persistence.
NOTE Confidence: 0.7937471722222222

00:51:39.476 --> 00:51:41.971 And I'll just say this is a this
NOTE Confidence: 0.7937471722222222

00:51:41.971 --> 00:51:43.346 is a super complicated study
NOTE Confidence: 0.7937471722222222

00:51:43.346 --> 00:51:45.240 with lots and lots of expertise.
NOTE Confidence: 0.7937471722222222

00:51:45.240 --> 00:51:48.006 These are only some of the
NOTE Confidence: 0.7937471722222222

00:51:48.006 --> 00:51:49.850 collaborators unsteady worldwide and.

NOTE Confidence: 0.793747172222222

00:51:49.850 --> 00:51:51.668 We'd be really lucky to have

NOTE Confidence: 0.793747172222222

00:51:51.668 --> 00:51:53.016 collaboration of some investigators

NOTE Confidence: 0.793747172222222

00:51:53.016 --> 00:51:54.488 in Department of Psychiatry.

NOTE Confidence: 0.793747172222222

00:51:54.490 --> 00:51:56.190 Whoever you really interested in

NOTE Confidence: 0.793747172222222

00:51:56.190 --> 00:51:58.230 working together with us on this.

NOTE Confidence: 0.793747172222222

00:51:58.230 --> 00:51:59.637 So I'm just going to show you

NOTE Confidence: 0.793747172222222

00:51:59.637 --> 00:52:00.480 some super preliminary data.

NOTE Confidence: 0.793747172222222

00:52:00.480 --> 00:52:01.888 We've presented 1 abstract

NOTE Confidence: 0.793747172222222

00:52:01.888 --> 00:52:03.648 based on this preliminary data,

NOTE Confidence: 0.793747172222222

00:52:03.650 --> 00:52:05.870 but we're really hoping to have

NOTE Confidence: 0.793747172222222

00:52:05.870 --> 00:52:08.282 about 100 patients to pull together

NOTE Confidence: 0.793747172222222

00:52:08.282 --> 00:52:10.427 for a more complete approach.

NOTE Confidence: 0.793747172222222

00:52:10.430 --> 00:52:13.546 I partly say that because this is

NOTE Confidence: 0.793747172222222

00:52:13.546 --> 00:52:15.286 a very heterogeneous condition and

NOTE Confidence: 0.793747172222222

00:52:15.286 --> 00:52:17.351 I think reporting on small numbers

NOTE Confidence: 0.793747172222222

00:52:17.351 --> 00:52:18.946 of people will not necessarily
NOTE Confidence: 0.7937471722222222

00:52:18.946 --> 00:52:21.098 give us the answers that we need.
NOTE Confidence: 0.7937471722222222

00:52:21.100 --> 00:52:22.730 But the first thirty four
NOTE Confidence: 0.7937471722222222

00:52:22.730 --> 00:52:24.360 people enrolled in our cohort,
NOTE Confidence: 0.7937471722222222

00:52:24.360 --> 00:52:28.306 our young age 5374% women 300
NOTE Confidence: 0.7937471722222222

00:52:28.306 --> 00:52:29.914 days from symptom onset.
NOTE Confidence: 0.7937471722222222

00:52:29.920 --> 00:52:32.958 So almost a year after acute COVID,
NOTE Confidence: 0.7937471722222222

00:52:32.960 --> 00:52:35.300 74% of them convalesced at home,
NOTE Confidence: 0.7937471722222222

00:52:35.300 --> 00:52:37.274 and the vast majority of them came
NOTE Confidence: 0.7937471722222222

00:52:37.274 --> 00:52:39.850 to us and rolled in our study
NOTE Confidence: 0.7937471722222222

00:52:39.850 --> 00:52:41.514 because of cognitive impairment.
NOTE Confidence: 0.7937471722222222

00:52:41.520 --> 00:52:44.660 59% also have mood symptoms,
NOTE Confidence: 0.7937471722222222

00:52:44.660 --> 00:52:46.753 and we're comparing them to pre pandemic
NOTE Confidence: 0.7937471722222222

00:52:46.753 --> 00:52:48.619 controls in the data that I'm going
NOTE Confidence: 0.7937471722222222

00:52:48.619 --> 00:52:50.958 to show you in the next couple of slides,
NOTE Confidence: 0.7937471722222222

00:52:50.960 --> 00:52:52.651 who were of a similar age, but.

NOTE Confidence: 0.793747172222222

00:52:52.651 --> 00:52:54.215 Different gender because most

NOTE Confidence: 0.793747172222222

00:52:54.215 --> 00:52:56.170 of our controls are men.

NOTE Confidence: 0.793747172222222

00:52:56.170 --> 00:52:57.773 So what are the kinds of symptoms

NOTE Confidence: 0.793747172222222

00:52:57.773 --> 00:52:59.348 these patients had during acute COVID?

NOTE Confidence: 0.793747172222222

00:52:59.350 --> 00:53:02.073 You can see it's all across the

NOTE Confidence: 0.793747172222222

00:53:02.073 --> 00:53:04.339 books and some of them had.

NOTE Confidence: 0.793747172222222

00:53:04.340 --> 00:53:05.390 Most of them had cough,

NOTE Confidence: 0.793747172222222

00:53:05.390 --> 00:53:06.545 fever and headache.

NOTE Confidence: 0.793747172222222

00:53:06.545 --> 00:53:09.240 Many of them also had other symptoms.

NOTE Confidence: 0.793747172222222

00:53:09.240 --> 00:53:10.220 Many people ask me well,

NOTE Confidence: 0.793747172222222

00:53:10.220 --> 00:53:11.796 did everybody have loss of taste and smell?

NOTE Confidence: 0.793747172222222

00:53:11.800 --> 00:53:14.080 Know in our study only 40% of these

NOTE Confidence: 0.793747172222222

00:53:14.080 --> 00:53:16.300 people who are having long term

NOTE Confidence: 0.793747172222222

00:53:16.300 --> 00:53:18.357 symptoms actually had a nausea or

NOTE Confidence: 0.793747172222222

00:53:18.357 --> 00:53:20.148 or thusia during acute COVID and

NOTE Confidence: 0.793747172222222

00:53:20.148 --> 00:53:21.516 what are the symptoms that they
NOTE Confidence: 0.793747172222222

00:53:21.516 --> 00:53:22.460 are now presenting with?
NOTE Confidence: 0.793747172222222

00:53:22.460 --> 00:53:24.971 We do a very very detailed survey of what
NOTE Confidence: 0.793747172222222

00:53:24.971 --> 00:53:27.457 kinds of symptoms people are experiencing,
NOTE Confidence: 0.793747172222222

00:53:27.460 --> 00:53:29.340 so you'll see lots of things on here.
NOTE Confidence: 0.793747172222222

00:53:29.340 --> 00:53:30.735 I think we've actually left
NOTE Confidence: 0.793747172222222

00:53:30.735 --> 00:53:32.466 off psychosis which a couple of
NOTE Confidence: 0.793747172222222

00:53:32.466 --> 00:53:33.876 people have also had psychosis,
NOTE Confidence: 0.793747172222222

00:53:33.880 --> 00:53:34.780 but you can see that.
NOTE Confidence: 0.793747172222222

00:53:34.780 --> 00:53:36.970 The majority of people are now
NOTE Confidence: 0.793747172222222

00:53:36.970 --> 00:53:38.430 having what they describe
NOTE Confidence: 0.811268676153846

00:53:38.503 --> 00:53:40.664 as cognitive impairment, anxiety,
NOTE Confidence: 0.811268676153846

00:53:40.664 --> 00:53:43.040 depression, fatigue and headache,
NOTE Confidence: 0.811268676153846

00:53:43.040 --> 00:53:44.896 and then some of these patients also have
NOTE Confidence: 0.811268676153846

00:53:44.896 --> 00:53:46.829 some of these other types of symptoms.
NOTE Confidence: 0.832369560769231

00:53:48.850 --> 00:53:50.170 So what I'm going to show you were

NOTE Confidence: 0.832369560769231

00:53:50.170 --> 00:53:51.598 just some really preliminary findings,

NOTE Confidence: 0.832369560769231

00:53:51.600 --> 00:53:52.758 and in all of these figures,

NOTE Confidence: 0.832369560769231

00:53:52.760 --> 00:53:54.950 the post COVID participants again

NOTE Confidence: 0.832369560769231

00:53:54.950 --> 00:53:57.632 about a year after having COVID-19

NOTE Confidence: 0.832369560769231

00:53:57.632 --> 00:54:00.340 a median time are shown in the red

NOTE Confidence: 0.832369560769231

00:54:00.340 --> 00:54:02.280 and our pre pandemic control samples

NOTE Confidence: 0.832369560769231

00:54:02.280 --> 00:54:04.270 who are basically healthy controls

NOTE Confidence: 0.832369560769231

00:54:04.270 --> 00:54:06.882 that were recruited for each of these

NOTE Confidence: 0.832369560769231

00:54:06.882 --> 00:54:08.424 studies are shown in the orange and

NOTE Confidence: 0.832369560769231

00:54:08.424 --> 00:54:10.308 what you can see here is we've looked

NOTE Confidence: 0.832369560769231

00:54:10.308 --> 00:54:11.838 at sort of different categories of

NOTE Confidence: 0.832369560769231

00:54:11.885 --> 00:54:13.369 markers and preliminary studies.

NOTE Confidence: 0.832369560769231

00:54:13.370 --> 00:54:15.170 These are immune measures that we

NOTE Confidence: 0.832369560769231

00:54:15.170 --> 00:54:16.695 wondered whether might be abnormal

NOTE Confidence: 0.832369560769231

00:54:16.695 --> 00:54:18.309 in the people who had COVID.

NOTE Confidence: 0.832369560769231

00:54:18.310 --> 00:54:20.934 And you can see that the only one
NOTE Confidence: 0.832369560769231

00:54:20.934 --> 00:54:22.486 that's persistently abnormal a year
NOTE Confidence: 0.832369560769231

00:54:22.486 --> 00:54:24.870 after COVID seems to be the D dimer,
NOTE Confidence: 0.832369560769231

00:54:24.870 --> 00:54:26.630 which is only slightly elevated
NOTE Confidence: 0.832369560769231

00:54:26.630 --> 00:54:29.162 and seems to be driven by small
NOTE Confidence: 0.832369560769231

00:54:29.162 --> 00:54:30.814 numbers of people. Do you die?
NOTE Confidence: 0.832369560769231

00:54:30.814 --> 00:54:32.002 Mark is a sort of general
NOTE Confidence: 0.832369560769231

00:54:32.002 --> 00:54:32.940 acute phase reactant,
NOTE Confidence: 0.832369560769231

00:54:32.940 --> 00:54:34.872 but it's also of course a marker
NOTE Confidence: 0.832369560769231

00:54:34.872 --> 00:54:36.569 of clotting and microphone by,
NOTE Confidence: 0.832369560769231

00:54:36.570 --> 00:54:38.025 so that's potentially a little
NOTE Confidence: 0.832369560769231

00:54:38.025 --> 00:54:40.049 hint of what could be going on.
NOTE Confidence: 0.832369560769231

00:54:40.050 --> 00:54:42.378 And then we've also had a nice collaboration
NOTE Confidence: 0.832369560769231

00:54:42.378 --> 00:54:44.928 to look at neuronal and astrocyte markers,
NOTE Confidence: 0.832369560769231

00:54:44.930 --> 00:54:47.218 and what we were surprised to find is
NOTE Confidence: 0.832369560769231

00:54:47.218 --> 00:54:49.137 that although most of these neuronal.

NOTE Confidence: 0.832369560769231
00:54:49.140 --> 00:54:51.947 Matt astrocyte markers NFL and Tau were
NOTE Confidence: 0.832369560769231
00:54:51.947 --> 00:54:54.558 normal or similar between the groups.
NOTE Confidence: 0.832369560769231
00:54:54.560 --> 00:54:56.583 We did find a hint of astrocyte
NOTE Confidence: 0.832369560769231
00:54:56.583 --> 00:54:59.038 injury in the blood and these people
NOTE Confidence: 0.832369560769231
00:54:59.038 --> 00:55:01.312 with long term symptoms after COVID.
NOTE Confidence: 0.832369560769231
00:55:01.320 --> 00:55:02.700 What exactly that means and where
NOTE Confidence: 0.832369560769231
00:55:02.700 --> 00:55:04.260 this GF AP is coming from?
NOTE Confidence: 0.832369560769231
00:55:04.260 --> 00:55:05.534 Is it definitely coming from the brain,
NOTE Confidence: 0.832369560769231
00:55:05.540 --> 00:55:07.256 or could it be coming from
NOTE Confidence: 0.832369560769231
00:55:07.256 --> 00:55:08.680 peripheral nerves in some way?
NOTE Confidence: 0.832369560769231
00:55:08.680 --> 00:55:10.000 Or some other kind of cell
NOTE Confidence: 0.832369560769231
00:55:10.000 --> 00:55:11.359 tech that we're not aware of?
NOTE Confidence: 0.832369560769231
00:55:11.360 --> 00:55:12.832 Is it interesting question?
NOTE Confidence: 0.832369560769231
00:55:12.832 --> 00:55:15.471 But this would be interpreted as actually
NOTE Confidence: 0.832369560769231
00:55:15.471 --> 00:55:17.643 being injury to astrocytes in the
NOTE Confidence: 0.832369560769231

00:55:17.643 --> 00:55:20.208 brain that we're detecting in the blood.

NOTE Confidence: 0.832369560769231

00:55:20.210 --> 00:55:21.536 We've also looked at spinal fluid

NOTE Confidence: 0.832369560769231

00:55:21.536 --> 00:55:23.010 in all of these individuals,

NOTE Confidence: 0.832369560769231

00:55:23.010 --> 00:55:24.648 so again these are really generous

NOTE Confidence: 0.832369560769231

00:55:24.648 --> 00:55:25.740 participants who are coming

NOTE Confidence: 0.832369560769231

00:55:25.791 --> 00:55:26.847 in for lumbar punctures,

NOTE Confidence: 0.832369560769231

00:55:26.850 --> 00:55:28.040 and you can see here that the

NOTE Confidence: 0.832369560769231

00:55:28.040 --> 00:55:28.989 white cell counts are normal.

NOTE Confidence: 0.832369560769231

00:55:28.990 --> 00:55:30.215 This is consistent with all

NOTE Confidence: 0.832369560769231

00:55:30.215 --> 00:55:30.950 the clinical experience,

NOTE Confidence: 0.832369560769231

00:55:30.950 --> 00:55:32.414 even during acute COVID.

NOTE Confidence: 0.832369560769231

00:55:32.414 --> 00:55:34.610 The protein albumin ratio when marker

NOTE Confidence: 0.832369560769231

00:55:34.670 --> 00:55:36.500 blood brain barrier are normal.

NOTE Confidence: 0.832369560769231

00:55:36.500 --> 00:55:38.552 We did find a higher percentage

NOTE Confidence: 0.832369560769231

00:55:38.552 --> 00:55:40.770 of monocytes in the CSF and

NOTE Confidence: 0.832369560769231

00:55:40.770 --> 00:55:42.690 individuals that have are still

NOTE Confidence: 0.832369560769231
00:55:42.690 --> 00:55:44.190 experiencing symptoms after COVID,
NOTE Confidence: 0.832369560769231
00:55:44.190 --> 00:55:45.840 so we're investigating that with more
NOTE Confidence: 0.832369560769231
00:55:45.840 --> 00:55:47.350 detailed solely on their studies,
NOTE Confidence: 0.832369560769231
00:55:47.350 --> 00:55:49.492 but it may be a hint that there's still
NOTE Confidence: 0.832369560769231
00:55:49.492 --> 00:55:51.358 some cellular immune perturbation.
NOTE Confidence: 0.832369560769231
00:55:51.360 --> 00:55:53.838 And finally, looking at the neuronal
NOTE Confidence: 0.832369560769231
00:55:53.838 --> 00:55:55.077 and astrocyte measures,
NOTE Confidence: 0.832369560769231
00:55:55.080 --> 00:55:57.420 we do see elevations in GF,
NOTE Confidence: 0.832369560769231
00:55:57.420 --> 00:56:00.957 AP and NFL in a couple of the people,
NOTE Confidence: 0.832369560769231
00:56:00.960 --> 00:56:03.310 but we're not seeing significantly
NOTE Confidence: 0.832369560769231
00:56:03.310 --> 00:56:05.320 different levels in the CSF.
NOTE Confidence: 0.832369560769231
00:56:05.320 --> 00:56:06.475 In these people,
NOTE Confidence: 0.832369560769231
00:56:06.480 --> 00:56:08.820 we're seeing a hint to elevations
NOTE Confidence: 0.832369560769231
00:56:08.820 --> 00:56:10.380 and CSF S tream,
NOTE Confidence: 0.832369560769231
00:56:10.380 --> 00:56:13.236 which is a microglial activation marker,
NOTE Confidence: 0.832369560769231

00:56:13.240 --> 00:56:14.716 but again, you can see why.
NOTE Confidence: 0.832369560769231

00:56:14.720 --> 00:56:16.670 I feel strongly that before we
NOTE Confidence: 0.832369560769231

00:56:16.670 --> 00:56:18.898 report any of this to the world,
NOTE Confidence: 0.832369560769231

00:56:18.900 --> 00:56:20.120 we really need more people.
NOTE Confidence: 0.832369560769231

00:56:20.120 --> 00:56:21.728 You can see there's a lot of heterogeneity.
NOTE Confidence: 0.832369560769231

00:56:21.730 --> 00:56:23.970 Here and we need to understand what
NOTE Confidence: 0.832369560769231

00:56:23.970 --> 00:56:25.724 are these patterns are persisting
NOTE Confidence: 0.832369560769231

00:56:25.724 --> 00:56:27.544 in larger numbers of people.
NOTE Confidence: 0.822511573333333

00:56:27.550 --> 00:56:28.000 Interestingly,
NOTE Confidence: 0.822511573333333

00:56:28.000 --> 00:56:30.637 we're seeing persistence of SARS, Co.
NOTE Confidence: 0.822511573333333

00:56:30.637 --> 00:56:33.346 V2 antibodies in the CSF and almost
NOTE Confidence: 0.822511573333333

00:56:33.346 --> 00:56:35.420 everybody that we're looking at.
NOTE Confidence: 0.822511573333333

00:56:35.420 --> 00:56:37.388 You expect the anti spike antibody
NOTE Confidence: 0.822511573333333

00:56:37.388 --> 00:56:40.169 on the top to be positive and
NOTE Confidence: 0.822511573333333

00:56:40.169 --> 00:56:42.080 everyone who's vaccinated and it
NOTE Confidence: 0.822511573333333

00:56:42.080 --> 00:56:43.865 does seem to be positive but the

NOTE Confidence: 0.8225115733333333

00:56:43.865 --> 00:56:45.924 anti nucleocapsid antibody is not

NOTE Confidence: 0.8225115733333333

00:56:45.924 --> 00:56:48.099 something that turns positive with

NOTE Confidence: 0.8225115733333333

00:56:48.099 --> 00:56:49.807 vaccination and that is persistently

NOTE Confidence: 0.8225115733333333

00:56:49.807 --> 00:56:51.898 positive in the CSF and the blood.

NOTE Confidence: 0.8225115733333333

00:56:51.898 --> 00:56:53.566 And and most of the people

NOTE Confidence: 0.8225115733333333

00:56:53.566 --> 00:56:54.620 that we've looked at,

NOTE Confidence: 0.8225115733333333

00:56:54.620 --> 00:56:57.524 so it's kind of interesting to see that

NOTE Confidence: 0.8225115733333333

00:56:57.524 --> 00:57:00.040 these antiviral antibodies are persisting,

NOTE Confidence: 0.8225115733333333

00:57:00.040 --> 00:57:02.122 and we're doing now additional studies

NOTE Confidence: 0.8225115733333333

00:57:02.122 --> 00:57:03.950 to look for evidence of autoimmunity.

NOTE Confidence: 0.8225115733333333

00:57:03.950 --> 00:57:06.143 So I'm going to end by a comparison

NOTE Confidence: 0.8225115733333333

00:57:06.143 --> 00:57:08.045 between two viruses that now I've

NOTE Confidence: 0.8225115733333333

00:57:08.045 --> 00:57:09.679 been studied for a long time.

NOTE Confidence: 0.8225115733333333

00:57:09.680 --> 00:57:10.884 Just to give you a sense of

NOTE Confidence: 0.8225115733333333

00:57:10.884 --> 00:57:11.560 how stars could be,

NOTE Confidence: 0.8225115733333333

00:57:11.560 --> 00:57:13.330 2 might be different than other
NOTE Confidence: 0.8225115733333333

00:57:13.330 --> 00:57:14.510 viruses that we understand.
NOTE Confidence: 0.8225115733333333

00:57:14.510 --> 00:57:16.980 So in general acute HIV,
NOTE Confidence: 0.8225115733333333

00:57:16.980 --> 00:57:18.070 which is really something that
NOTE Confidence: 0.8225115733333333

00:57:18.070 --> 00:57:19.420 we've been studying for many years,
NOTE Confidence: 0.8225115733333333

00:57:19.420 --> 00:57:21.842 looking at the first weeks and months
NOTE Confidence: 0.8225115733333333

00:57:21.842 --> 00:57:25.010 after initial HIV entry into the body,
NOTE Confidence: 0.8225115733333333

00:57:25.010 --> 00:57:27.596 is associated with robust viral invasion.
NOTE Confidence: 0.8225115733333333

00:57:27.600 --> 00:57:30.400 This can be detected in the CSF.
NOTE Confidence: 0.8225115733333333

00:57:30.400 --> 00:57:32.157 This can be detected in the brain,
NOTE Confidence: 0.8225115733333333

00:57:32.160 --> 00:57:33.774 whereas servers could be 2 does
NOTE Confidence: 0.8225115733333333

00:57:33.774 --> 00:57:35.580 not seem to have significant.
NOTE Confidence: 0.8225115733333333

00:57:35.580 --> 00:57:36.126 Viral invasion,
NOTE Confidence: 0.8225115733333333

00:57:36.126 --> 00:57:38.310 at least it does not seem to be
NOTE Confidence: 0.8225115733333333

00:57:38.376 --> 00:57:40.296 something that's detectable at the level
NOTE Confidence: 0.8225115733333333

00:57:40.296 --> 00:57:42.858 of CSF or most brain tissue studies.

NOTE Confidence: 0.8225115733333333
00:57:42.860 --> 00:57:43.326 However,
NOTE Confidence: 0.8225115733333333
00:57:43.326 --> 00:57:46.122 both viruses seem to be associated
NOTE Confidence: 0.8225115733333333
00:57:46.122 --> 00:57:48.600 with immune cell trafficking to
NOTE Confidence: 0.8225115733333333
00:57:48.600 --> 00:57:51.095 the CNS and immune activation,
NOTE Confidence: 0.8225115733333333
00:57:51.100 --> 00:57:52.186 so generalized neuroinflammation
NOTE Confidence: 0.8225115733333333
00:57:52.186 --> 00:57:53.996 I mentioned the fact that
NOTE Confidence: 0.8225115733333333
00:57:53.996 --> 00:57:55.559 there's changes in siding kinds.
NOTE Confidence: 0.8225115733333333
00:57:55.560 --> 00:57:58.748 There's also microglial activation
NOTE Confidence: 0.8225115733333333
00:57:58.748 --> 00:58:01.936 in brain autopsy tissues.
NOTE Confidence: 0.8225115733333333
00:58:01.940 --> 00:58:03.450 Autoimmune responses do occur in
NOTE Confidence: 0.8225115733333333
00:58:03.450 --> 00:58:05.266 some people with acute HIV and
NOTE Confidence: 0.8225115733333333
00:58:05.266 --> 00:58:06.988 it's kind of one of those hallmarks
NOTE Confidence: 0.8225115733333333
00:58:06.988 --> 00:58:08.664 that you teach residents to look
NOTE Confidence: 0.8225115733333333
00:58:08.664 --> 00:58:10.356 for acute HIV and somebody with
NOTE Confidence: 0.8225115733333333
00:58:10.360 --> 00:58:12.270 Jan Murray and emergency room.
NOTE Confidence: 0.8225115733333333

00:58:12.270 --> 00:58:14.670 But in fact this seems to be something
NOTE Confidence: 0.8225115733333333

00:58:14.670 --> 00:58:16.858 we're seeing frequently in acute COVID.
NOTE Confidence: 0.8225115733333333

00:58:16.860 --> 00:58:18.337 And is that because we just have
NOTE Confidence: 0.8225115733333333

00:58:18.337 --> 00:58:19.818 billions of cases of COVID worldwide,
NOTE Confidence: 0.8225115733333333

00:58:19.820 --> 00:58:21.620 so we're seeing these conditions more?
NOTE Confidence: 0.8225115733333333

00:58:21.620 --> 00:58:22.995 Or is there actually something
NOTE Confidence: 0.8225115733333333

00:58:22.995 --> 00:58:24.770 about this virus that is more
NOTE Confidence: 0.8225115733333333

00:58:24.770 --> 00:58:26.170 prone to trigger autoimmunity?
NOTE Confidence: 0.8225115733333333

00:58:26.170 --> 00:58:28.039 And so I think it's a super
NOTE Confidence: 0.8225115733333333

00:58:28.039 --> 00:58:28.573 important question.
NOTE Confidence: 0.8225115733333333

00:58:28.580 --> 00:58:30.035 Acute thrombosis and stroke is
NOTE Confidence: 0.8225115733333333

00:58:30.035 --> 00:58:31.848 a feature of acute COVID which
NOTE Confidence: 0.8225115733333333

00:58:31.848 --> 00:58:33.348 is different than acute HIV.
NOTE Confidence: 0.8225115733333333

00:58:33.350 --> 00:58:35.384 So it really relates to something
NOTE Confidence: 0.8225115733333333

00:58:35.384 --> 00:58:37.708 particular about how this virus activates
NOTE Confidence: 0.8225115733333333

00:58:37.708 --> 00:58:39.968 endothelial cells and clotting systems.

NOTE Confidence: 0.8225115733333333

00:58:39.970 --> 00:58:42.268 Nerdy generation seems to be detectable

NOTE Confidence: 0.8225115733333333

00:58:42.268 --> 00:58:44.650 in some people with acute COVID.

NOTE Confidence: 0.8225115733333333

00:58:44.650 --> 00:58:47.530 We also see this in acute infection with HIV.

NOTE Confidence: 0.8225115733333333

00:58:47.530 --> 00:58:48.965 So what are going to be the

NOTE Confidence: 0.8225115733333333

00:58:48.965 --> 00:58:49.950 long term consequences of this?

NOTE Confidence: 0.8225115733333333

00:58:49.950 --> 00:58:51.470 I think we don't know.

NOTE Confidence: 0.8225115733333333

00:58:51.470 --> 00:58:52.990 Clearly HIV is a persistent

NOTE Confidence: 0.8225115733333333

00:58:52.990 --> 00:58:54.819 infection as I explained the viral

NOTE Confidence: 0.8225115733333333

00:58:54.819 --> 00:58:56.569 life cycle is one that you get

NOTE Confidence: 0.8225115733333333

00:58:56.569 --> 00:58:58.493 long term infection of host cells

NOTE Confidence: 0.8225115733333333

00:58:58.493 --> 00:59:00.203 because the virus integrates its

NOTE Confidence: 0.8225115733333333

00:59:00.203 --> 00:59:01.978 genome into our host cells.

NOTE Confidence: 0.8225115733333333

00:59:01.978 --> 00:59:03.763 This is hopefully not true.

NOTE Confidence: 0.8225115733333333

00:59:03.770 --> 00:59:04.994 Instars kovi 2.

NOTE Confidence: 0.8225115733333333

00:59:04.994 --> 00:59:07.442 We don't even see initial infection,

NOTE Confidence: 0.8225115733333333

00:59:07.450 --> 00:59:09.310 so hopefully it's not persistent infection,
NOTE Confidence: 0.8225115733333333

00:59:09.310 --> 00:59:11.347 but that doesn't mean there isn't persistent.
NOTE Confidence: 0.8225115733333333

00:59:11.350 --> 00:59:13.348 Antigen presence and I think that's
NOTE Confidence: 0.8225115733333333

00:59:13.348 --> 00:59:14.680 a really important distinction
NOTE Confidence: 0.8225115733333333

00:59:14.734 --> 00:59:16.349 and important area for research.
NOTE Confidence: 0.84228417

00:59:16.350 --> 00:59:18.065 Long term neurologic sequella is
NOTE Confidence: 0.84228417

00:59:18.065 --> 00:59:19.780 clearly something that happens when
NOTE Confidence: 0.84228417

00:59:19.831 --> 00:59:21.643 you set up infection and inflammation
NOTE Confidence: 0.84228417

00:59:21.643 --> 00:59:23.110 in reservoirs in acute HIV,
NOTE Confidence: 0.84228417

00:59:23.110 --> 00:59:24.657 but I think the question of whether
NOTE Confidence: 0.84228417

00:59:24.657 --> 00:59:26.847 or not this is going to be a long term
NOTE Confidence: 0.84228417

00:59:26.847 --> 00:59:28.216 problem and people with acute starts
NOTE Confidence: 0.84228417

00:59:28.216 --> 00:59:30.850 could be too still needs to be answered.
NOTE Confidence: 0.84228417

00:59:30.850 --> 00:59:32.026 So I'm going to end by just saying,
NOTE Confidence: 0.84228417

00:59:32.030 --> 00:59:33.590 you know, these are the gaps and questions.
NOTE Confidence: 0.84228417

00:59:33.590 --> 00:59:35.207 Why do we still need to learn?

NOTE Confidence: 0.84228417

00:59:35.210 --> 00:59:36.800 I think the really pressing questions

NOTE Confidence: 0.84228417

00:59:36.800 --> 00:59:38.732 now relate to long COVID and these

NOTE Confidence: 0.84228417

00:59:38.732 --> 00:59:40.650 lingering effects of people who are really

NOTE Confidence: 0.84228417

00:59:40.705 --> 00:59:42.409 having trouble getting back to work.

NOTE Confidence: 0.84228417

00:59:42.410 --> 00:59:44.380 I'm having trouble functioning having

NOTE Confidence: 0.84228417

00:59:44.380 --> 00:59:47.669 very little to turn in terms of therapies,

NOTE Confidence: 0.84228417

00:59:47.670 --> 00:59:49.931 so we need to understand the biological

NOTE Confidence: 0.84228417

00:59:49.931 --> 00:59:52.169 mechanisms of these long ongoing symptoms.

NOTE Confidence: 0.84228417

00:59:52.170 --> 00:59:54.585 One possibility is this is due to

NOTE Confidence: 0.84228417

00:59:54.585 --> 00:59:56.550 injury occurred during two infection.

NOTE Confidence: 0.84228417

00:59:56.550 --> 00:59:58.182 I will say I do not think this

NOTE Confidence: 0.84228417

00:59:58.182 --> 00:59:59.090 is the problem.

NOTE Confidence: 0.84228417

00:59:59.090 --> 01:00:01.386 I think many people who have severe

NOTE Confidence: 0.84228417

01:00:01.386 --> 01:00:03.522 disease during acute infection recover

NOTE Confidence: 0.84228417

01:00:03.522 --> 01:00:05.834 completely and then some people who have

NOTE Confidence: 0.84228417

01:00:05.834 --> 01:00:08.382 mild disease who don't seem to have had
NOTE Confidence: 0.84228417

01:00:08.382 --> 01:00:10.022 neurologic symptoms even during that
NOTE Confidence: 0.84228417

01:00:10.022 --> 01:00:12.389 time seemed to have persistent symptoms.
NOTE Confidence: 0.84228417

01:00:12.390 --> 01:00:13.758 But of course we need to
NOTE Confidence: 0.84228417

01:00:13.758 --> 01:00:14.670 be studying that more.
NOTE Confidence: 0.84228417

01:00:14.670 --> 01:00:17.010 Another possibility is ongoing perturbations
NOTE Confidence: 0.84228417

01:00:17.010 --> 01:00:19.350 and inflammation and immune responses,
NOTE Confidence: 0.84228417

01:00:19.350 --> 01:00:21.492 and I think this is one of the major
NOTE Confidence: 0.84228417

01:00:21.492 --> 01:00:22.948 hypothesis for long COVID overall,
NOTE Confidence: 0.84228417

01:00:22.950 --> 01:00:24.222 and I think as it relates
NOTE Confidence: 0.84228417

01:00:24.222 --> 01:00:25.070 to the nervous system,
NOTE Confidence: 0.84228417

01:00:25.070 --> 01:00:26.252 we have a lot of evidence
NOTE Confidence: 0.84228417

01:00:26.252 --> 01:00:27.310 that that might be true.
NOTE Confidence: 0.84228417

01:00:27.310 --> 01:00:29.776 Can there be a vascular inflammation
NOTE Confidence: 0.84228417

01:00:29.776 --> 01:00:31.420 or microvascular compromise that's
NOTE Confidence: 0.84228417

01:00:31.485 --> 01:00:33.195 continuing to have impacts on

NOTE Confidence: 0.84228417

01:00:33.195 --> 01:00:35.321 blood flow and brain function even

NOTE Confidence: 0.84228417

01:00:35.321 --> 01:00:37.106 after recovery from acute COVID?

NOTE Confidence: 0.84228417

01:00:37.110 --> 01:00:37.790 And finally,

NOTE Confidence: 0.84228417

01:00:37.790 --> 01:00:39.830 is there a possibility that there's

NOTE Confidence: 0.84228417

01:00:39.830 --> 01:00:41.735 low level viral antigen either

NOTE Confidence: 0.84228417

01:00:41.735 --> 01:00:43.279 in the endothelial cells?

NOTE Confidence: 0.84228417

01:00:43.280 --> 01:00:45.604 Wanting them to blood vessels in the

NOTE Confidence: 0.84228417

01:00:45.604 --> 01:00:48.077 brain or actually in brain tissue itself,

NOTE Confidence: 0.84228417

01:00:48.080 --> 01:00:50.232 and I think this is still an area

NOTE Confidence: 0.84228417

01:00:50.232 --> 01:00:52.000 that needs to be investigated.

NOTE Confidence: 0.84228417

01:00:52.000 --> 01:00:53.320 And I'll end by talking about,

NOTE Confidence: 0.84228417

01:00:53.320 --> 01:00:54.120 you know this is a.

NOTE Confidence: 0.84228417

01:00:54.120 --> 01:00:55.836 This is a pretty vulnerable population.

NOTE Confidence: 0.84228417

01:00:55.840 --> 01:00:57.268 I spent my career taking care

NOTE Confidence: 0.84228417

01:00:57.268 --> 01:00:58.220 of people with HIV.

NOTE Confidence: 0.84228417

01:00:58.220 --> 01:00:59.069 And you know,
NOTE Confidence: 0.84228417

01:00:59.069 --> 01:00:59.918 this is it's.
NOTE Confidence: 0.84228417

01:00:59.920 --> 01:01:02.139 It's been a highly recognized for a
NOTE Confidence: 0.84228417

01:01:02.139 --> 01:01:04.150 really long time that people living
NOTE Confidence: 0.84228417

01:01:04.150 --> 01:01:06.460 with HIV are vulnerable to lots and
NOTE Confidence: 0.84228417

01:01:06.522 --> 01:01:08.490 lots of different social and other
NOTE Confidence: 0.84228417

01:01:08.490 --> 01:01:10.622 kinds of challenges that make living
NOTE Confidence: 0.84228417

01:01:10.622 --> 01:01:12.462 with illness even more difficult.
NOTE Confidence: 0.84228417

01:01:12.470 --> 01:01:14.294 And I would say that there are ways
NOTE Confidence: 0.84228417

01:01:14.294 --> 01:01:16.420 in which long COVID also has a lot
NOTE Confidence: 0.84228417

01:01:16.420 --> 01:01:17.920 of personal challenges for people.
NOTE Confidence: 0.84228417

01:01:17.920 --> 01:01:19.132 There's stigma associated with
NOTE Confidence: 0.84228417

01:01:19.132 --> 01:01:19.738 this condition.
NOTE Confidence: 0.84228417

01:01:19.740 --> 01:01:20.985 There's a lack of understanding
NOTE Confidence: 0.84228417

01:01:20.985 --> 01:01:22.230 a lot of people are.
NOTE Confidence: 0.84228417

01:01:22.230 --> 01:01:23.990 Really frustrated and how a lack of hope

NOTE Confidence: 0.84228417

01:01:23.990 --> 01:01:25.489 that things are going to get better,

NOTE Confidence: 0.84228417

01:01:25.490 --> 01:01:27.002 so I think this is really why we

NOTE Confidence: 0.84228417

01:01:27.002 --> 01:01:28.743 have such a research mandate to try

NOTE Confidence: 0.84228417

01:01:28.743 --> 01:01:30.053 to understand this condition and

NOTE Confidence: 0.84228417

01:01:30.098 --> 01:01:31.946 hopefully see that it resolves over time,

NOTE Confidence: 0.84228417

01:01:31.950 --> 01:01:34.281 but if not to develop their therapeutic

NOTE Confidence: 0.84228417

01:01:34.281 --> 01:01:36.074 interventions that are targeted to

NOTE Confidence: 0.84228417

01:01:36.074 --> 01:01:37.914 and really writing these conditions.

NOTE Confidence: 0.84228417

01:01:37.920 --> 01:01:41.440 So end by thanking all of our colleagues.

NOTE Confidence: 0.84228417

01:01:41.440 --> 01:01:43.176 Thank you so much for the invitation.

NOTE Confidence: 0.84228417

01:01:43.180 --> 01:01:44.926 Thank you in participant to the

NOTE Confidence: 0.84228417

01:01:44.926 --> 01:01:46.090 general study participants who

NOTE Confidence: 0.804293125333333

01:01:46.145 --> 01:01:47.790 were coming in for these studies in

NOTE Confidence: 0.804293125333333

01:01:47.790 --> 01:01:49.532 the setting of all the uncertainty

NOTE Confidence: 0.804293125333333

01:01:49.532 --> 01:01:50.848 they're experiencing and to

NOTE Confidence: 0.804293125333333

01:01:50.848 --> 01:01:52.893 particularly to Shelly and Lindsey who

NOTE Confidence: 0.804293125333333

01:01:52.893 --> 01:01:55.350 are Co directing the study with me.

NOTE Confidence: 0.804293125333333

01:01:55.350 --> 01:01:57.464 I will stop sharing so that I

NOTE Confidence: 0.804293125333333

01:01:57.464 --> 01:01:59.409 can see people for questions.

NOTE Confidence: 0.804293125333333

01:01:59.410 --> 01:02:01.996 Thanks so much for the attention.