WEBVTT

NOTE duration: ”00:47:54.581”

NOTE Confidence: 0.95499265

00:00:00.080 --> 00:00:01.040 Alright. Well, thank you so

NOTE Confidence: 0.95499265

00:00:01.040 --> 00:00:02.080 much. Let me just a

NOTE Confidence: 0.95499265

00:00:02.080 --> 00:00:03.919 brief introduction to myself. I'm

NOTE Confidence: 0.95499265

00:00:03.919 --> 00:00:05.040 a research scientist here at

NOTE Confidence: 0.95499265

00:00:05.040 --> 00:00:06.640 Yale University, Department of OB

NOTE Confidence: 0.95499265

00:00:06.640 --> 00:00:07.140 GYN.

NOTE Confidence: 0.9791951

00:00:08.160 --> 00:00:09.200 I've been here at Yale

NOTE Confidence: 0.9791951

00:00:09.200 --> 00:00:10.900 for thirty four years proudly,

NOTE Confidence: 0.9791951

00:00:11.119 --> 00:00:12.320 and I'm proud to be

NOTE Confidence: 0.9791951

00:00:12.320 --> 00:00:13.219 part of the GPRPL

NOTE Confidence: 0.9905772

00:00:13.519 --> 00:00:14.019 study.

NOTE Confidence: 0.96755254

00:00:15.245 --> 00:00:16.685 I have always been very

NOTE Confidence: 0.96755254

00:00:16.685 --> 00:00:18.285 enthusiastic about this study and,

NOTE Confidence: 0.96755254

00:00:18.285 --> 00:00:19.485 from the very beginning, wanted

NOTE Confidence: 0.96755254

00:00:19.485 --> 00:00:20.925 to be involved because this

NOTE Confidence: 0.96755254

00:00:20.925 --> 00:00:21.805 is what I deal with

NOTE Confidence: 0.96755254

00:00:21.805 --> 00:00:22.305 clinically.

NOTE Confidence: 0.9790507

00:00:22.845 --> 00:00:23.805 And I thought I would

NOTE Confidence: 0.9790507

00:00:23.805 --> 00:00:24.305 share,

NOTE Confidence: 0.99727505

00:00:25.485 --> 00:00:26.525 the work that we've been

NOTE Confidence: 0.99727505

00:00:26.525 --> 00:00:28.605 doing related to pregnancy loss,

NOTE Confidence: 0.99727505

00:00:28.765 --> 00:00:29.904 looking at the placenta,

NOTE Confidence: 0.9216268

00:00:30.260 --> 00:00:31.720 and how all these things

NOTE Confidence: 0.9216268

00:00:31.780 --> 00:00:32.920 in my mind,

NOTE Confidence: 0.97387075

00:00:33.460 --> 00:00:35.159 come together in a unifying

NOTE Confidence: 0.97387075

00:00:35.300 --> 00:00:37.720 hypothesis related to trophoblast inclusions,

NOTE Confidence: 0.9928613

00:00:38.180 --> 00:00:39.460 which I will introduce to

NOTE Confidence: 0.9928613

00:00:39.460 --> 00:00:40.820 you. I always like to

NOTE Confidence: 0.9928613

00:00:40.820 --> 00:00:42.659 start I'm, again, a physician

NOTE Confidence: 0.9928613

00:00:42.659 --> 00:00:43.860 scientist, so I take care

NOTE Confidence: 0.9928613

00:00:43.860 --> 00:00:45.080 of patients, do research.

NOTE Confidence: 0.96704257

00:00:45.704 --> 00:00:46.504 I always like to start

NOTE Confidence: 0.96704257

00:00:46.504 --> 00:00:47.784 off with my patients because

NOTE Confidence: 0.96704257

00:00:47.784 --> 00:00:48.664 I think it gives a

NOTE Confidence: 0.96704257

00:00:48.664 --> 00:00:50.184 context of what we're dealing

NOTE Confidence: 0.96704257

00:00:50.184 --> 00:00:51.805 with. So this is NH,

NOTE Confidence: 0.96704257

00:00:51.864 --> 00:00:52.664 at the time that I

NOTE Confidence: 0.96704257

00:00:52.664 --> 00:00:53.625 met her, a thirty year

NOTE Confidence: 0.96704257

00:00:53.625 --> 00:00:54.364 old G3P1,

NOTE Confidence: 0.99414945

00:00:55.464 --> 00:00:57.245 one stillbirth and two miscarriages,

NOTE Confidence: 0.99414945

00:00:57.385 --> 00:00:59.290 no living children. Her first

NOTE Confidence: 0.99414945

00:00:59.290 --> 00:01:00.970 loss here in twenty seventeen

NOTE Confidence: 0.99414945

00:01:00.970 --> 00:01:02.490 was thirty two weeks and

NOTE Confidence: 0.99414945

00:01:02.490 --> 00:01:03.150 two days

NOTE Confidence: 0.9302823

00:01:03.530 --> 00:01:05.150 of stillbirth. What was notable

NOTE Confidence: 0.9302823

00:01:05.370 --> 00:01:06.730 is the placenta was at

NOTE Confidence: 0.9302823

00:01:06.730 --> 00:01:07.390 the point

NOTE Confidence: 0.91018474

00:01:07.930 --> 00:01:08.910 one percentile,

NOTE Confidence: 0.96825784

00:01:09.290 --> 00:01:10.030 very small.

NOTE Confidence: 0.97730017

00:01:10.650 --> 00:01:11.770 This is from an outside

NOTE Confidence: 0.97730017

00:01:11.770 --> 00:01:12.270 institution.

NOTE Confidence: 0.95926

00:01:12.650 --> 00:01:13.530 It was sent to me

NOTE Confidence: 0.95926

00:01:13.530 --> 00:01:15.415 as a consult. The outside

NOTE Confidence: 0.95926

00:01:15.415 --> 00:01:17.335 institution, the pathology basically just

NOTE Confidence: 0.95926

00:01:17.335 --> 00:01:19.515 said normal placenta, normal karyotype,

NOTE Confidence: 0.95926

00:01:19.815 --> 00:01:21.335 and she was told, these

NOTE Confidence: 0.95926

00:01:21.335 --> 00:01:23.115 things happen. Just try again.

NOTE Confidence: 0.99763507

00:01:23.655 --> 00:01:24.935 So they did try again.

NOTE Confidence: 0.99763507

00:01:24.935 --> 00:01:26.615 Infertility is not their issue.

NOTE Confidence: 0.99763507

00:01:26.615 --> 00:01:28.055 They got pregnant again fairly

NOTE Confidence: 0.99763507

00:01:28.055 --> 00:01:28.555 easily.

NOTE Confidence: 0.98013866

00:01:28.910 --> 00:01:30.190 They had a sixteen week

NOTE Confidence: 0.98013866

00:01:30.190 --> 00:01:31.410 loss, now a miscarriage.

NOTE Confidence: 0.9699269

00:01:32.270 --> 00:01:34.110 At this point, the classic

NOTE Confidence: 0.9699269

00:01:34.110 --> 00:01:36.190 diagnosis by pathologists of products

NOTE Confidence: 0.9699269

00:01:36.190 --> 00:01:37.709 of conception, which has no

NOTE Confidence: 0.9699269

00:01:37.709 --> 00:01:39.230 information at all to it,

NOTE Confidence: 0.9699269

00:01:39.230 --> 00:01:40.350 we knew it was products

NOTE Confidence: 0.9699269

00:01:40.350 --> 00:01:41.550 of conception, so it's not

NOTE Confidence: 0.9699269

00:01:41.550 --> 00:01:43.075 helpful to have that as

NOTE Confidence: 0.9699269

00:01:43.075 --> 00:01:44.275 the diagnosis, but this is

NOTE Confidence: 0.9699269

00:01:44.275 --> 00:01:45.475 what they were told. And

NOTE Confidence: 0.9699269

00:01:45.475 --> 00:01:47.155 again, these things happen, try

NOTE Confidence: 0.9699269

00:01:47.155 --> 00:01:47.655 again.

NOTE Confidence: 0.92138654

00:01:47.955 --> 00:01:49.075 So they did, they got

NOTE Confidence: 0.92138654

00:01:49.075 --> 00:01:50.515 pregnant yet again and had

NOTE Confidence: 0.92138654

00:01:50.515 --> 00:01:51.635 at this point a twelve

NOTE Confidence: 0.92138654

00:01:51.635 --> 00:01:52.455 week miscarriage.

NOTE Confidence: 0.9810466

00:01:52.915 --> 00:01:54.835 Again, products of conception were

NOTE Confidence: 0.9810466

00:01:54.835 --> 00:01:56.460 diagnosed and they were simply

NOTE Confidence: 0.9810466

00:01:56.460 --> 00:01:58.140 told to try again. Well,

NOTE Confidence: 0.9810466

00:01:58.140 --> 00:01:59.180 as you can imagine, this

NOTE Confidence: 0.9810466

00:01:59.180 --> 00:02:00.620 was very frustrating, so they

NOTE Confidence: 0.9810466

00:02:00.620 --> 00:02:02.300 did find another resource and

NOTE Confidence: 0.9810466

00:02:02.300 --> 00:02:04.240 luckily found out about me,

NOTE Confidence: 0.9810466

00:02:04.460 --> 00:02:05.740 sent me their entire case

NOTE Confidence: 0.9810466

00:02:05.740 --> 00:02:07.340 for review, and I looked

NOTE Confidence: 0.9810466

00:02:07.340 --> 00:02:08.860 at all these placentas and

NOTE Confidence: 0.9810466

00:02:08.860 --> 00:02:09.900 found that there were no

NOTE Confidence: 0.9810466

00:02:09.900 --> 00:02:12.425 clots, no immune responses, no

NOTE Confidence: 0.9810466

00:02:12.425 --> 00:02:13.565 bacterial responses.

NOTE Confidence: 0.9914258

00:02:14.264 --> 00:02:15.645 So what is going on?

NOTE Confidence: 0.9524353

00:02:16.025 --> 00:02:17.625 Why have the has this

NOTE Confidence: 0.9524353

00:02:17.625 --> 00:02:19.085 couple had these three losses?

NOTE Confidence: 0.99801165

00:02:19.385 --> 00:02:20.345 So we'll get back to

NOTE Confidence: 0.99801165

00:02:20.345 --> 00:02:21.225 them in a minute, but

NOTE Confidence: 0.99801165

00:02:21.225 --> 00:02:22.105 let me pull back and

NOTE Confidence: 0.99801165

00:02:22.105 --> 00:02:23.225 just give an overview in

NOTE Confidence: 0.99801165

00:02:23.225 --> 00:02:24.605 terms of pregnancy losses.

NOTE Confidence: 0.9821211

00:02:25.020 --> 00:02:27.120 There are five million pregnancies

NOTE Confidence: 0.9821211

00:02:27.180 --> 00:02:28.319 a year in our country.

NOTE Confidence: 0.96431273

00:02:28.780 --> 00:02:30.400 There are four million liveborns

NOTE Confidence: 0.6308417

00:02:30.700 --> 00:02:31.200 approximately.

NOTE Confidence: 0.9467633

00:02:31.660 --> 00:02:32.620 That means that there are

NOTE Confidence: 0.9467633

00:02:32.620 --> 00:02:34.300 a million pregnancy losses. So

NOTE Confidence: 0.9467633

00:02:34.300 --> 00:02:35.340 that is a very large

NOTE Confidence: 0.9467633

00:02:35.340 --> 00:02:35.840 number.

NOTE Confidence: 0.95647955

00:02:37.044 --> 00:02:38.485 The majority of these are

NOTE Confidence: 0.95647955

00:02:38.485 --> 00:02:40.245 miscarriages, and we define these

NOTE Confidence: 0.95647955

00:02:40.245 --> 00:02:41.605 in our country as variable

NOTE Confidence: 0.95647955

00:02:41.605 --> 00:02:42.905 from country to country

NOTE Confidence: 0.9687305

00:02:43.284 --> 00:02:44.644 as a loss less than

NOTE Confidence: 0.9687305

00:02:44.644 --> 00:02:45.864 twenty weeks of gestation.

NOTE Confidence: 0.98799634

00:02:46.165 --> 00:02:47.364 And I'll point out in

NOTE Confidence: 0.98799634

00:02:47.364 --> 00:02:48.405 a few minutes that this

NOTE Confidence: 0.98799634

00:02:48.405 --> 00:02:50.084 is an arbitrary division. I

NOTE Confidence: 0.98799634

00:02:50.084 --> 00:02:51.364 don't think it's exactly the

NOTE Confidence: 0.98799634

00:02:51.364 --> 00:02:51.870 right place

NOTE Confidence: 0.9500334

00:02:52.430 --> 00:02:52.750 that we should have this

NOTE Confidence: 0.9500334

00:02:52.750 --> 00:02:53.250 division,

NOTE Confidence: 0.94635785

00:02:53.790 --> 00:02:55.069 but this is the way

NOTE Confidence: 0.94635785

00:02:55.069 --> 00:02:56.209 it is for us now.

NOTE Confidence: 0.94635785

00:02:56.349 --> 00:02:58.110 And we define losses a

NOTE Confidence: 0.94635785

00:02:58.110 --> 00:02:59.549 greater equal or greater than

NOTE Confidence: 0.94635785

00:02:59.549 --> 00:03:00.830 twenty weeks as a stillbirth,

NOTE Confidence: 0.94635785

00:03:00.830 --> 00:03:01.870 and there are about twenty

NOTE Confidence: 0.94635785

00:03:01.870 --> 00:03:03.409 three thousand in our country.

NOTE Confidence: 0.9839542

00:03:04.595 --> 00:03:05.794 One of the frustrating things

NOTE Confidence: 0.9839542

00:03:05.794 --> 00:03:07.395 about pregnancy losses is that

NOTE Confidence: 0.9839542

00:03:07.395 --> 00:03:07.895 for

NOTE Confidence: 0.9733712

00:03:08.355 --> 00:03:10.275 decades, the unexplained rate, in

NOTE Confidence: 0.9733712

00:03:10.275 --> 00:03:11.395 other words, the rate at

NOTE Confidence: 0.9733712

00:03:11.395 --> 00:03:12.995 which losses could not be

NOTE Confidence: 0.9733712

00:03:12.995 --> 00:03:14.595 explained and no cause could

NOTE Confidence: 0.9733712

00:03:14.595 --> 00:03:16.115 be attributed to them, has

NOTE Confidence: 0.9733712

00:03:16.115 --> 00:03:18.115 remained about constant, about thirty

NOTE Confidence: 0.9733712

00:03:18.115 --> 00:03:19.540 percent for years. So So

NOTE Confidence: 0.9733712

00:03:19.540 --> 00:03:20.500 we haven't really put a

NOTE Confidence: 0.9733712

00:03:20.500 --> 00:03:21.400 dent in this.

NOTE Confidence: 0.9774048

00:03:21.780 --> 00:03:23.060 And the question is, why

NOTE Confidence: 0.9774048

00:03:23.060 --> 00:03:24.180 is that? Why can't we

NOTE Confidence: 0.9774048

00:03:24.180 --> 00:03:25.380 figure out what's going on

NOTE Confidence: 0.9774048

00:03:25.380 --> 00:03:26.760 with these pregnancy losses?

NOTE Confidence: 0.9211343

00:03:27.460 --> 00:03:28.580 And I think the reason

NOTE Confidence: 0.9211343

00:03:28.580 --> 00:03:29.080 is

NOTE Confidence: 0.94937897

00:03:29.460 --> 00:03:29.960 simple.

NOTE Confidence: 0.9751056

00:03:30.260 --> 00:03:32.520 One is routine pathologic examination

NOTE Confidence: 0.9925436

00:03:32.900 --> 00:03:34.735 of the losses often doesn't

NOTE Confidence: 0.9925436

00:03:34.735 --> 00:03:36.735 reveal a pathologic problem, as

NOTE Confidence: 0.9925436

00:03:36.735 --> 00:03:37.715 these three cases

NOTE Confidence: 0.98403925

00:03:38.415 --> 00:03:40.515 show you, and current standard

NOTE Confidence: 0.98403925

00:03:40.655 --> 00:03:42.915 genetic analyses are not sufficient

NOTE Confidence: 0.98403925

00:03:42.974 --> 00:03:44.334 to find out a genetic

NOTE Confidence: 0.98403925

00:03:44.334 --> 00:03:44.834 reason.

NOTE Confidence: 0.9775349

00:03:45.215 --> 00:03:46.860 Now, of course, a routine

NOTE Confidence: 0.9775349

00:03:46.920 --> 00:03:47.800 thing is to get a

NOTE Confidence: 0.9775349

00:03:47.800 --> 00:03:49.640 karyotype and a microarray, for

NOTE Confidence: 0.9775349

00:03:49.640 --> 00:03:50.140 example,

NOTE Confidence: 0.9864748

00:03:50.680 --> 00:03:51.880 and many of my patients

NOTE Confidence: 0.9864748

00:03:51.880 --> 00:03:53.240 are very confused when they

NOTE Confidence: 0.9864748

00:03:53.240 --> 00:03:54.920 have a result that returns

NOTE Confidence: 0.9864748

00:03:54.920 --> 00:03:56.300 back as a normal karyotype

NOTE Confidence: 0.9864748

00:03:56.360 --> 00:03:57.020 or microarray,

NOTE Confidence: 0.9971731

00:03:57.560 --> 00:03:58.780 they feel that their

NOTE Confidence: 0.95675564

00:03:59.160 --> 00:04:01.224 pregnancy loss was not due

NOTE Confidence: 0.95675564

00:04:01.224 --> 00:04:03.065 to a genetic abnormality. But

NOTE Confidence: 0.95675564

00:04:03.065 --> 00:04:04.105 as we know, that is

NOTE Confidence: 0.95675564

00:04:04.105 --> 00:04:05.625 not true. Even if a

NOTE Confidence: 0.95675564

00:04:05.625 --> 00:04:07.565 karyotype and microarray are normal,

NOTE Confidence: 0.95675564

00:04:07.705 --> 00:04:09.144 there still obviously can be

NOTE Confidence: 0.95675564

00:04:09.144 --> 00:04:10.205 a genetic abnormality.

NOTE Confidence: 0.9532923

00:04:10.584 --> 00:04:11.864 And the reason is, is

NOTE Confidence: 0.9532923

00:04:11.864 --> 00:04:13.885 there are six billion DNA

NOTE Confidence: 0.9532923

00:04:13.944 --> 00:04:14.444 codes

NOTE Confidence: 0.973636

00:04:14.985 --> 00:04:16.044 in our genome.

NOTE Confidence: 0.9555201

00:04:17.380 --> 00:04:19.000 And our goal for GPRPL

NOTE Confidence: 0.9555201

00:04:19.220 --> 00:04:20.100 is to try to solve

NOTE Confidence: 0.9555201

00:04:20.100 --> 00:04:21.060 this problem. So this is

NOTE Confidence: 0.9555201

00:04:21.060 --> 00:04:22.660 the underlying goal for our

NOTE Confidence: 0.9555201

00:04:22.660 --> 00:04:24.020 project and what brings us

NOTE Confidence: 0.9555201

00:04:24.020 --> 00:04:24.680 all together.

NOTE Confidence: 0.9828522

00:04:25.140 --> 00:04:26.660 In the meantime, while we're

NOTE Confidence: 0.9828522

00:04:26.660 --> 00:04:28.120 trying to figure that out,

NOTE Confidence: 0.9828522

00:04:28.180 --> 00:04:29.700 I have been asking myself

NOTE Confidence: 0.9828522

00:04:29.700 --> 00:04:30.915 for the last three decades,

NOTE Confidence: 0.9828522

00:04:30.915 --> 00:04:32.435 Is there another way to

NOTE Confidence: 0.9828522

00:04:32.435 --> 00:04:34.214 diagnose a genetic abnormality

NOTE Confidence: 0.9968063

00:04:34.675 --> 00:04:35.495 in a pregnancy?

NOTE Confidence: 0.97410923

00:04:36.435 --> 00:04:37.955 And obviously, one doesn't ask

NOTE Confidence: 0.97410923

00:04:37.955 --> 00:04:38.995 a question unless you have

NOTE Confidence: 0.97410923

00:04:38.995 --> 00:04:40.355 an answer for it. And

NOTE Confidence: 0.97410923

00:04:40.355 --> 00:04:41.475 I do believe there is

NOTE Confidence: 0.97410923

00:04:41.475 --> 00:04:43.380 a way to answer that.

NOTE Confidence: 0.97410923

00:04:43.540 --> 00:04:44.500 And the way to do

NOTE Confidence: 0.97410923

00:04:44.500 --> 00:04:45.460 it is by looking at

NOTE Confidence: 0.97410923

00:04:45.460 --> 00:04:47.320 the placenta and identify

NOTE Confidence: 0.99948156

00:04:47.700 --> 00:04:49.800 dysmorphic features in the placenta.

NOTE Confidence: 0.9878101

00:04:50.180 --> 00:04:51.380 Well, in order to teach

NOTE Confidence: 0.9878101

00:04:51.380 --> 00:04:52.980 you about dysmorphic features in

NOTE Confidence: 0.9878101

00:04:52.980 --> 00:04:54.180 the placenta, I just want

NOTE Confidence: 0.9878101

00:04:54.180 --> 00:04:55.620 to remind people about the

NOTE Confidence: 0.9878101

00:04:55.620 --> 00:04:57.080 normal structure of the placenta.

NOTE Confidence: 0.9878101

00:04:57.365 --> 00:04:58.725 Maybe it's familiar to many

NOTE Confidence: 0.9878101

00:04:58.725 --> 00:04:59.525 of you, but for those

NOTE Confidence: 0.9878101

00:04:59.525 --> 00:05:00.805 that aren't, I'm just going

NOTE Confidence: 0.9878101

00:05:00.805 --> 00:05:01.765 to give a very brief,

NOTE Confidence: 0.9878101

00:05:02.085 --> 00:05:04.665 embryologic overview here of ovulation,

NOTE Confidence: 0.9878101

00:05:04.885 --> 00:05:05.385 fertilization,

NOTE Confidence: 0.97023076

00:05:06.245 --> 00:05:06.985 early embryological

NOTE Confidence: 0.9537465

00:05:07.445 --> 00:05:07.945 development,

NOTE Confidence: 0.99600375

00:05:08.485 --> 00:05:10.265 and attachment of this blastocyst

NOTE Confidence: 0.99600375

00:05:10.404 --> 00:05:11.525 to the lining of the

NOTE Confidence: 0.99600375

00:05:11.525 --> 00:05:12.665 uterus, the endometrium.

NOTE Confidence: 0.9869377

00:05:13.700 --> 00:05:15.560 About nine days after fertilization,

NOTE Confidence: 0.9869377

00:05:15.780 --> 00:05:16.840 this is what a pregnancy

NOTE Confidence: 0.9869377

00:05:16.900 --> 00:05:18.760 looks like, the little embryo

NOTE Confidence: 0.9869377

00:05:18.820 --> 00:05:20.020 has now turned into a

NOTE Confidence: 0.9869377

00:05:20.020 --> 00:05:21.480 little three layer embryo,

NOTE Confidence: 0.99513745

00:05:21.860 --> 00:05:23.300 and the single layer of

NOTE Confidence: 0.99513745

00:05:23.300 --> 00:05:25.060 trophoblasts, which will become the

NOTE Confidence: 0.99513745

00:05:25.060 --> 00:05:25.560 placenta,

NOTE Confidence: 0.98643655

00:05:25.865 --> 00:05:27.785 have now differentiated into two

NOTE Confidence: 0.98643655

00:05:27.785 --> 00:05:29.085 different types of trophoblasts,

NOTE Confidence: 0.96263146

00:05:29.625 --> 00:05:30.445 the cytotrophoblasts,

NOTE Confidence: 0.98439264

00:05:30.985 --> 00:05:32.265 which is the stem cell,

NOTE Confidence: 0.98439264

00:05:32.265 --> 00:05:33.785 the inner layer, and the

NOTE Confidence: 0.98439264

00:05:33.785 --> 00:05:35.325 outer layer, the syncytiotrophoblasts,

NOTE Confidence: 0.95156854

00:05:36.585 --> 00:05:37.325 a multinucleoid

NOTE Confidence: 0.94851685

00:05:37.785 --> 00:05:39.305 cell that, for example, at

NOTE Confidence: 0.94851685

00:05:39.305 --> 00:05:40.925 this point in pregnancy is

NOTE Confidence: 0.94851685

00:05:41.220 --> 00:05:43.240 making large quantities of hCG.

NOTE Confidence: 0.99418

00:05:43.940 --> 00:05:45.220 So this is what things

NOTE Confidence: 0.99418

00:05:45.220 --> 00:05:46.440 look like at that point.

NOTE Confidence: 0.99418

00:05:46.580 --> 00:05:48.339 If we jump ahead to

NOTE Confidence: 0.99418

00:05:48.339 --> 00:05:50.120 the third trimester, for example,

NOTE Confidence: 0.98029345

00:05:50.500 --> 00:05:51.860 this is the overall structure

NOTE Confidence: 0.98029345

00:05:51.860 --> 00:05:53.460 of the placenta. The fetus

NOTE Confidence: 0.98029345

00:05:53.460 --> 00:05:55.035 would be up here, connected

NOTE Confidence: 0.98029345

00:05:55.035 --> 00:05:56.315 to its placenta through its

NOTE Confidence: 0.98029345

00:05:56.315 --> 00:05:58.235 umbilical cord. You can think

NOTE Confidence: 0.98029345

00:05:58.235 --> 00:05:59.595 of the placenta as the

NOTE Confidence: 0.98029345

00:05:59.595 --> 00:06:00.875 root system of a tree.

NOTE Confidence: 0.98029345

00:06:00.875 --> 00:06:01.755 So if you can see

NOTE Confidence: 0.98029345

00:06:01.755 --> 00:06:03.675 my hand, imagine my hand

NOTE Confidence: 0.98029345

00:06:03.675 --> 00:06:04.794 in a bucket of water

NOTE Confidence: 0.98029345

00:06:04.794 --> 00:06:06.495 with my fingers wiggling around,

NOTE Confidence: 0.98029345

00:06:06.680 --> 00:06:07.880 That's what the villus tree

NOTE Confidence: 0.98029345

00:06:07.880 --> 00:06:09.480 looks like. The water in

NOTE Confidence: 0.98029345

00:06:09.480 --> 00:06:11.080 this analogy is mom's blood,

NOTE Confidence: 0.98029345

00:06:11.080 --> 00:06:12.520 which is fountaining like a

NOTE Confidence: 0.98029345

00:06:12.520 --> 00:06:14.700 sprinkler system into the placenta.

NOTE Confidence: 0.98695844

00:06:15.400 --> 00:06:17.080 Let's dive down and look

NOTE Confidence: 0.98695844

00:06:17.080 --> 00:06:18.360 at a little more detail

NOTE Confidence: 0.98695844

00:06:18.360 --> 00:06:19.800 the structure of the villus

NOTE Confidence: 0.98695844

00:06:19.800 --> 00:06:21.645 trophoblasts here. So if we

NOTE Confidence: 0.98695844

00:06:21.645 --> 00:06:22.605 pull out one of these

NOTE Confidence: 0.98695844

00:06:22.605 --> 00:06:24.525 single villi, the fingers that

NOTE Confidence: 0.98695844

00:06:24.525 --> 00:06:26.045 I just showed you, and

NOTE Confidence: 0.98695844

00:06:26.045 --> 00:06:27.325 you cut a knife through

NOTE Confidence: 0.98695844

00:06:27.325 --> 00:06:28.605 it, you start to see

NOTE Confidence: 0.98695844

00:06:28.605 --> 00:06:30.365 the cellular structure of the

NOTE Confidence: 0.98695844

00:06:30.365 --> 00:06:31.885 villus and you see the

NOTE Confidence: 0.98695844

00:06:31.885 --> 00:06:33.404 same exact cells that I

NOTE Confidence: 0.98695844

00:06:33.404 --> 00:06:34.305 showed you before.

NOTE Confidence: 0.98227966

00:06:34.620 --> 00:06:36.480 The inner layer, the cytotrophoblast,

NOTE Confidence: 0.9859139

00:06:36.940 --> 00:06:38.140 is the stem cell, the

NOTE Confidence: 0.9859139

00:06:38.140 --> 00:06:39.980 proliferative cell, and the outer

NOTE Confidence: 0.9859139

00:06:39.980 --> 00:06:41.200 layer, the syncytiotrophoblast.

NOTE Confidence: 0.99254084

00:06:42.460 --> 00:06:43.900 You can consider this the

NOTE Confidence: 0.99254084

00:06:43.900 --> 00:06:45.279 working cell of the placenta,

NOTE Confidence: 0.9685165

00:06:45.580 --> 00:06:47.279 makes all the hormones, mediates

NOTE Confidence: 0.9685165

00:06:47.339 --> 00:06:49.120 transports, and things like that.

NOTE Confidence: 0.97937363

00:06:50.245 --> 00:06:51.525 This is a diagram. This

NOTE Confidence: 0.97937363

00:06:51.525 --> 00:06:52.985 is what a third trimester

NOTE Confidence: 0.97882617

00:06:53.444 --> 00:06:55.125 cross section of chorionic villi

NOTE Confidence: 0.97882617

00:06:55.125 --> 00:06:56.645 would look like. The white

NOTE Confidence: 0.97882617

00:06:56.645 --> 00:06:58.005 space is where mom's blood

NOTE Confidence: 0.97882617

00:06:58.005 --> 00:06:59.845 would be, the skin covering,

NOTE Confidence: 0.97882617

00:06:59.845 --> 00:07:00.805 if you will, of the

NOTE Confidence: 0.97882617

00:07:00.805 --> 00:07:02.985 fingers of the trophoblast layer,

NOTE Confidence: 0.97882617

00:07:03.139 --> 00:07:04.419 and you can see the

NOTE Confidence: 0.97882617

00:07:04.419 --> 00:07:06.020 fetal capillaries with the fetal

NOTE Confidence: 0.97882617

00:07:06.020 --> 00:07:07.320 red blood cells inside.

NOTE Confidence: 0.98065734

00:07:07.940 --> 00:07:09.940 Now, anybody who has done

NOTE Confidence: 0.98065734

00:07:09.940 --> 00:07:11.380 pediatrics or has had a

NOTE Confidence: 0.98065734

00:07:11.380 --> 00:07:13.220 baby or knows anything about

NOTE Confidence: 0.98065734

00:07:13.220 --> 00:07:14.419 what happens in labor and

NOTE Confidence: 0.98065734

00:07:14.419 --> 00:07:15.880 delivery room after delivery,

NOTE Confidence: 0.99829

00:07:16.255 --> 00:07:17.775 you know that the first

NOTE Confidence: 0.99829

00:07:17.775 --> 00:07:18.815 thing that we do when

NOTE Confidence: 0.99829

00:07:18.815 --> 00:07:19.795 we look at a newborn

NOTE Confidence: 0.99829

00:07:19.855 --> 00:07:21.635 baby is try to identify

NOTE Confidence: 0.99829

00:07:21.935 --> 00:07:22.435 dysmorphic

NOTE Confidence: 0.99953794

00:07:22.735 --> 00:07:23.235 features.

NOTE Confidence: 0.99346703

00:07:23.615 --> 00:07:24.815 Why do we do that?

NOTE Confidence: 0.99346703

00:07:24.815 --> 00:07:26.275 Because this is the easiest

NOTE Confidence: 0.99346703

00:07:26.335 --> 00:07:28.015 way, just with a visual

NOTE Confidence: 0.99346703

00:07:28.015 --> 00:07:28.515 inspection,

NOTE Confidence: 0.99852026

00:07:28.895 --> 00:07:29.855 to give a hint that

NOTE Confidence: 0.99852026

00:07:29.855 --> 00:07:30.995 there might be a genetic

NOTE Confidence: 0.99852026

00:07:31.055 --> 00:07:31.555 abnormality.

NOTE Confidence: 0.98084015

00:07:32.150 --> 00:07:33.510 In this diagram, you can

NOTE Confidence: 0.98084015

00:07:33.510 --> 00:07:35.030 see trisomy twenty one at

NOTE Confidence: 0.98084015

00:07:35.030 --> 00:07:36.550 the top, trisomy eighteen in

NOTE Confidence: 0.98084015

00:07:36.550 --> 00:07:38.070 the middle, and trisomy thirteen

NOTE Confidence: 0.98084015

00:07:38.070 --> 00:07:39.770 at the bottom. These are

NOTE Confidence: 0.98084015

00:07:39.830 --> 00:07:41.510 pretty obvious and just from

NOTE Confidence: 0.98084015

00:07:41.510 --> 00:07:43.430 the dysmorphic features of these

NOTE Confidence: 0.98084015

00:07:43.430 --> 00:07:44.710 newborns, you can make these

NOTE Confidence: 0.98084015

00:07:44.710 --> 00:07:45.210 diagnoses.

NOTE Confidence: 0.9997126

00:07:45.910 --> 00:07:46.410 However,

NOTE Confidence: 0.96621424

00:07:47.155 --> 00:07:48.515 on the left are much

NOTE Confidence: 0.96621424

00:07:48.515 --> 00:07:51.255 more subtle developmental problems, dysmorphic

NOTE Confidence: 0.96621424

00:07:51.315 --> 00:07:52.755 features, in this case of

NOTE Confidence: 0.96621424

00:07:52.755 --> 00:07:53.575 hand development.

NOTE Confidence: 0.9868653

00:07:53.955 --> 00:07:55.315 And in these cases, these

NOTE Confidence: 0.9868653

00:07:55.315 --> 00:07:57.015 children have normal karyotypes,

NOTE Confidence: 0.9777889

00:07:57.395 --> 00:07:59.175 but they have genetic abnormalities.

NOTE Confidence: 0.9777889

00:07:59.395 --> 00:08:01.250 In fact, the genetic abnormalities

NOTE Confidence: 0.9777889

00:08:01.550 --> 00:08:02.770 to lead to polydactyly

NOTE Confidence: 0.9439657

00:08:03.070 --> 00:08:04.590 in these abnormal hand developments

NOTE Confidence: 0.9439657

00:08:04.590 --> 00:08:05.570 are quite interesting.

NOTE Confidence: 0.9991107

00:08:05.950 --> 00:08:07.570 They relate to the three-dimensional

NOTE Confidence: 0.9996736

00:08:08.030 --> 00:08:09.169 structure of the DNA

NOTE Confidence: 0.9935957

00:08:09.710 --> 00:08:11.070 of the ninety nine percent

NOTE Confidence: 0.9935957

00:08:11.070 --> 00:08:12.590 of the six billion codes

NOTE Confidence: 0.9935957

00:08:12.590 --> 00:08:14.110 that don't code for any

NOTE Confidence: 0.9935957

00:08:14.110 --> 00:08:15.465 genes that we know of.

NOTE Confidence: 0.9935957

00:08:15.544 --> 00:08:16.425 So this is just a

NOTE Confidence: 0.9935957

00:08:16.425 --> 00:08:18.125 little hint of the complexity

NOTE Confidence: 0.9935957

00:08:18.345 --> 00:08:19.165 of the genome.

NOTE Confidence: 0.9660146

00:08:19.705 --> 00:08:21.645 Now, just as newborn babies

NOTE Confidence: 0.9660146

00:08:21.705 --> 00:08:22.824 can be looked at for

NOTE Confidence: 0.9660146

00:08:22.824 --> 00:08:25.385 dysmorphic features, the placenta can

NOTE Confidence: 0.9660146

00:08:25.385 --> 00:08:26.505 also be looked at for

NOTE Confidence: 0.9660146

00:08:26.505 --> 00:08:28.620 dysmorphic features. And the placenta,

NOTE Confidence: 0.9660146

00:08:28.620 --> 00:08:29.740 as I pointed out, is

NOTE Confidence: 0.9660146

00:08:29.740 --> 00:08:31.259 like the root system, again,

NOTE Confidence: 0.9660146

00:08:31.259 --> 00:08:32.300 my hand in the bucket

NOTE Confidence: 0.9660146

00:08:32.300 --> 00:08:34.059 of water. Here's a diagram

NOTE Confidence: 0.9660146

00:08:34.059 --> 00:08:35.900 of the branching structure of

NOTE Confidence: 0.9660146

00:08:35.900 --> 00:08:37.580 the placenta, and most of

NOTE Confidence: 0.9660146

00:08:37.580 --> 00:08:39.740 the placenta basically forms by

NOTE Confidence: 0.9660146

00:08:39.740 --> 00:08:42.380 branching outward to create its

NOTE Confidence: 0.9660146

00:08:42.380 --> 00:08:42.880 structure.

NOTE Confidence: 0.99921507

00:08:43.385 --> 00:08:45.465 The dysmorphic feature we see

NOTE Confidence: 0.99921507

00:08:45.465 --> 00:08:46.285 in the placenta

NOTE Confidence: 0.99887687

00:08:46.745 --> 00:08:47.804 is an abnormal

NOTE Confidence: 0.8173067

00:08:48.184 --> 00:08:48.684 infolding.

NOTE Confidence: 0.9972273

00:08:49.304 --> 00:08:50.684 We call it an invagination.

NOTE Confidence: 0.9906661

00:08:51.785 --> 00:08:52.985 This is a diagram to

NOTE Confidence: 0.9906661

00:08:52.985 --> 00:08:53.865 the right. This is the

NOTE Confidence: 0.9906661

00:08:53.865 --> 00:08:54.985 real picture to the left.

NOTE Confidence: 0.9906661

00:08:54.985 --> 00:08:55.945 Let me focus on the

NOTE Confidence: 0.9906661

00:08:55.945 --> 00:08:56.445 diagram.

NOTE Confidence: 0.99512464

00:08:56.910 --> 00:08:58.190 It looks like someone has

NOTE Confidence: 0.99512464

00:08:58.190 --> 00:08:59.790 taken their finger and pushed

NOTE Confidence: 0.99512464

00:08:59.790 --> 00:09:01.570 inward to bend the bilayer

NOTE Confidence: 0.99512464

00:09:01.630 --> 00:09:03.309 inward. That's not what is

NOTE Confidence: 0.99512464

00:09:03.309 --> 00:09:05.230 happening. What is actually happening

NOTE Confidence: 0.99512464

00:09:05.230 --> 00:09:07.089 is there are too many

NOTE Confidence: 0.9973348

00:09:07.709 --> 00:09:08.209 cytotrophoblasts,

NOTE Confidence: 0.92821264

00:09:08.829 --> 00:09:09.889 these pink cells.

NOTE Confidence: 0.95328474

00:09:10.404 --> 00:09:12.425 Too much cell proliferation.

NOTE Confidence: 0.996924

00:09:13.125 --> 00:09:14.804 Just continue to remember that

NOTE Confidence: 0.996924

00:09:14.804 --> 00:09:15.765 as we go through this

NOTE Confidence: 0.996924

00:09:15.765 --> 00:09:17.765 presentation here. On the left,

NOTE Confidence: 0.996924

00:09:17.765 --> 00:09:19.525 you can see the piling

NOTE Confidence: 0.996924

00:09:19.525 --> 00:09:20.904 up of all these cytotrophoblasts

NOTE Confidence: 0.9818703

00:09:21.285 --> 00:09:22.885 in this focal area, and

NOTE Confidence: 0.9818703

00:09:22.885 --> 00:09:25.065 that bends the bilayer inward.

NOTE Confidence: 0.9884632

00:09:26.390 --> 00:09:27.910 If the knife happens to

NOTE Confidence: 0.9884632

00:09:27.910 --> 00:09:29.430 randomly cut across one of

NOTE Confidence: 0.9884632

00:09:29.430 --> 00:09:30.170 these invaginations,

NOTE Confidence: 0.976772

00:09:30.630 --> 00:09:32.410 like this SS cut here,

NOTE Confidence: 0.976772

00:09:32.630 --> 00:09:33.370 it creates

NOTE Confidence: 0.9933686

00:09:33.990 --> 00:09:35.610 what we call a trophoblast

NOTE Confidence: 0.99958956

00:09:35.990 --> 00:09:36.490 inclusion.

NOTE Confidence: 0.9275474

00:09:37.110 --> 00:09:37.610 Truphoblast

NOTE Confidence: 0.9301963

00:09:38.084 --> 00:09:38.584 invaginations

NOTE Confidence: 0.9985839

00:09:38.964 --> 00:09:40.985 and inclusions are the dysmorphic

NOTE Confidence: 0.9985839

00:09:41.204 --> 00:09:42.584 features of the placenta.

NOTE Confidence: 0.6937641

00:09:42.924 --> 00:09:43.424 So,

NOTE Confidence: 0.965926

00:09:43.925 --> 00:09:45.524 and again, just to highlight

NOTE Confidence: 0.965926

00:09:45.524 --> 00:09:46.404 this, and I'll show you

NOTE Confidence: 0.965926

00:09:46.404 --> 00:09:48.165 a three-dimensional reconstruction of this

NOTE Confidence: 0.965926

00:09:48.165 --> 00:09:49.365 in a minute, this is

NOTE Confidence: 0.965926

00:09:49.365 --> 00:09:50.550 actually the same structure,

NOTE Confidence: 0.854937

00:09:52.149 --> 00:09:53.110 just happens to be moving

NOTE Confidence: 0.854937

00:09:53.110 --> 00:09:53.589 in and out of the

NOTE Confidence: 0.854937

00:09:53.589 --> 00:09:54.470 plane of the section. So

NOTE Confidence: 0.854937

00:09:54.470 --> 00:09:55.929 this invagination is continuous

NOTE Confidence: 0.7946334

00:09:56.309 --> 00:09:57.429 with this cross section of

NOTE Confidence: 0.7946334

00:09:57.429 --> 00:09:59.670 this trophoblast inclusion. That's And

NOTE Confidence: 0.7946334

00:09:59.670 --> 00:10:01.510 you are sure. Go for

NOTE Confidence: 0.7946334

00:10:01.510 --> 00:10:02.870 the questions. So you get

NOTE Confidence: 0.7946334

00:10:02.870 --> 00:10:03.370 this

NOTE Confidence: 0.9396247

00:10:03.675 --> 00:10:05.195 excessive proliferation of cells. Why

NOTE Confidence: 0.9396247

00:10:05.195 --> 00:10:06.554 wouldn't they bulge outwards? Why

NOTE Confidence: 0.9396247

00:10:06.554 --> 00:10:07.535 does it always invaginate?

NOTE Confidence: 0.9881824

00:10:07.995 --> 00:10:09.455 Oh, what a good question.

NOTE Confidence: 0.9881824

00:10:09.755 --> 00:10:10.955 Well, it has to do

NOTE Confidence: 0.9881824

00:10:10.955 --> 00:10:13.215 with mechanical engineering and physics.

NOTE Confidence: 0.9851497

00:10:13.595 --> 00:10:15.515 So it depends on which

NOTE Confidence: 0.9851497

00:10:15.515 --> 00:10:17.480 side has more cells. I'm

NOTE Confidence: 0.9851497

00:10:17.480 --> 00:10:18.679 gonna give you an analogy.

NOTE Confidence: 0.9851497

00:10:18.679 --> 00:10:19.879 If you remember the hundred

NOTE Confidence: 0.9851497

00:10:19.879 --> 00:10:21.240 meter dash in the Olympics

NOTE Confidence: 0.9851497

00:10:21.240 --> 00:10:22.519 last summer, you know how

NOTE Confidence: 0.9851497

00:10:22.519 --> 00:10:24.040 they stagger all the runners

NOTE Confidence: 0.9851497

00:10:24.040 --> 00:10:25.319 in different places on the

NOTE Confidence: 0.9851497

00:10:25.319 --> 00:10:26.679 track. You can think of

NOTE Confidence: 0.9851497

00:10:26.679 --> 00:10:27.579 the cytotrophoblast

NOTE Confidence: 0.94859964

00:10:28.360 --> 00:10:30.540 lane here as a longer

NOTE Confidence: 0.94859964

00:10:30.759 --> 00:10:31.259 lane,

NOTE Confidence: 0.9765906

00:10:31.565 --> 00:10:32.605 and this is the outer

NOTE Confidence: 0.9765906

00:10:32.605 --> 00:10:33.885 lane of the tract, and

NOTE Confidence: 0.9765906

00:10:33.885 --> 00:10:35.265 this is the inner lane.

NOTE Confidence: 0.9765906

00:10:35.485 --> 00:10:36.684 So if there is more

NOTE Confidence: 0.9765906

00:10:36.684 --> 00:10:38.204 material on this side, it

NOTE Confidence: 0.9765906

00:10:38.204 --> 00:10:39.325 has to bend in this

NOTE Confidence: 0.9765906

00:10:39.325 --> 00:10:40.925 direction. If there was more

NOTE Confidence: 0.9765906

00:10:40.925 --> 00:10:42.545 material on the blue side,

NOTE Confidence: 0.9765906

00:10:42.605 --> 00:10:43.885 it would bend outward. And

NOTE Confidence: 0.9765906

00:10:43.885 --> 00:10:44.765 I will show you an

NOTE Confidence: 0.9765906

00:10:44.765 --> 00:10:46.030 example of that. So it

NOTE Confidence: 0.9765906

00:10:46.030 --> 00:10:48.450 just depends on the, basically,

NOTE Confidence: 0.9765906

00:10:48.510 --> 00:10:49.250 the kinetics

NOTE Confidence: 0.99404234

00:10:49.710 --> 00:10:51.470 of which layer has more

NOTE Confidence: 0.99404234

00:10:51.470 --> 00:10:52.830 cells in it. Either the

NOTE Confidence: 0.99404234

00:10:52.830 --> 00:10:53.950 inner layer or the outer

NOTE Confidence: 0.99404234

00:10:53.950 --> 00:10:55.790 layer determines which way things

NOTE Confidence: 0.99404234

00:10:55.790 --> 00:10:56.290 bend.

NOTE Confidence: 0.979798

00:10:56.750 --> 00:10:58.990 Great, insightful question. Thank you.

NOTE Confidence: 0.979798

00:10:58.990 --> 00:11:01.005 Now, I will just highlight

NOTE Confidence: 0.979798

00:11:01.005 --> 00:11:02.705 some more pictures of invaginations

NOTE Confidence: 0.97292024

00:11:03.085 --> 00:11:04.225 from other placentas.

NOTE Confidence: 0.97406286

00:11:04.765 --> 00:11:05.804 And this last one on

NOTE Confidence: 0.97406286

00:11:05.804 --> 00:11:07.085 the lower right, if anybody

NOTE Confidence: 0.97406286

00:11:07.085 --> 00:11:07.905 knows dermatology,

NOTE Confidence: 0.9339455

00:11:08.445 --> 00:11:09.804 you might remember something called

NOTE Confidence: 0.9339455

00:11:09.804 --> 00:11:12.065 an epidermal inclusion cyst. Sometimes

NOTE Confidence: 0.9339455

00:11:12.125 --> 00:11:13.485 it appears as a little

NOTE Confidence: 0.9339455

00:11:13.485 --> 00:11:15.300 bump on someone's face. That's

NOTE Confidence: 0.9339455

00:11:15.380 --> 00:11:16.279 from an invagination

NOTE Confidence: 0.99907285

00:11:16.580 --> 00:11:17.720 of the squamous

NOTE Confidence: 0.9702158

00:11:18.420 --> 00:11:19.779 lining of the skin, and

NOTE Confidence: 0.9702158

00:11:19.779 --> 00:11:21.140 then the skin continues to

NOTE Confidence: 0.9702158

00:11:21.140 --> 00:11:22.980 grow but inside of the

NOTE Confidence: 0.9702158

00:11:22.980 --> 00:11:24.899 dermis, basically. And this is

NOTE Confidence: 0.9702158

00:11:24.899 --> 00:11:27.080 like an epidermal inclusion cyst.

NOTE Confidence: 0.9702158

00:11:27.380 --> 00:11:28.980 Again, if the knife happens

NOTE Confidence: 0.9702158

00:11:28.980 --> 00:11:30.304 to cut across any of

NOTE Confidence: 0.9702158

00:11:30.304 --> 00:11:31.125 these invaginations,

NOTE Confidence: 0.99852943

00:11:31.905 --> 00:11:33.445 it appears as trophoblast

NOTE Confidence: 0.99964935

00:11:33.825 --> 00:11:34.325 inclusions.

NOTE Confidence: 0.97956157

00:11:35.105 --> 00:11:36.465 Well, one of the questions

NOTE Confidence: 0.97956157

00:11:36.465 --> 00:11:37.425 that I'm always asked is,

NOTE Confidence: 0.97956157

00:11:37.425 --> 00:11:38.385 Well, gee, are you the

NOTE Confidence: 0.97956157

00:11:38.385 --> 00:11:39.585 only one who sees this?

NOTE Confidence: 0.97956157

00:11:39.585 --> 00:11:40.545 Are you the first one

NOTE Confidence: 0.97956157

00:11:40.545 --> 00:11:42.240 to have seen this? Have

NOTE Confidence: 0.97956157

00:11:42.240 --> 00:11:43.679 other people seen this before?

NOTE Confidence: 0.97956157

00:11:43.679 --> 00:11:44.640 Are you living in a

NOTE Confidence: 0.97956157

00:11:44.640 --> 00:11:46.160 fantasy world? What's going on

NOTE Confidence: 0.97956157

00:11:46.160 --> 00:11:47.280 with you, Harvey? So I

NOTE Confidence: 0.97956157

00:11:47.280 --> 00:11:48.800 just wanna highlight a little

NOTE Confidence: 0.97956157

00:11:48.800 --> 00:11:50.640 history here that these were

NOTE Confidence: 0.97956157

00:11:50.640 --> 00:11:52.340 first seen in the eighteen

NOTE Confidence: 0.97956157

00:11:52.559 --> 00:11:53.059 hundreds.

NOTE Confidence: 0.90886045

00:11:53.600 --> 00:11:54.559 For those of you who

NOTE Confidence: 0.90886045

00:11:54.559 --> 00:11:56.420 read German, I'm gonna translate

NOTE Confidence: 0.90886045

00:11:56.480 --> 00:11:57.845 this. This is a Google

NOTE Confidence: 0.90886045

00:11:57.904 --> 00:12:00.404 translate here. Syncytial Geschwasellen

NOTE Confidence: 0.96629703

00:12:01.265 --> 00:12:03.505 are syncytial tumor cells. And

NOTE Confidence: 0.96629703

00:12:03.505 --> 00:12:05.524 here's an actual photo micrograph

NOTE Confidence: 0.96629703

00:12:05.665 --> 00:12:07.584 from eighteen ninety seven of

NOTE Confidence: 0.96629703

00:12:07.584 --> 00:12:09.184 a microscopic view of a

NOTE Confidence: 0.96629703

00:12:09.184 --> 00:12:11.040 placenta of a pregnancy loss

NOTE Confidence: 0.96629703

00:12:11.279 --> 00:12:12.660 in this journal.

NOTE Confidence: 0.91963214

00:12:13.199 --> 00:12:14.959 And the article, the title

NOTE Confidence: 0.91963214

00:12:14.959 --> 00:12:16.100 of the article is Malignant

NOTE Confidence: 0.91963214

00:12:16.160 --> 00:12:16.660 Deciduomas.

NOTE Confidence: 0.9576709

00:12:17.440 --> 00:12:18.240 You can kind of get

NOTE Confidence: 0.9576709

00:12:18.240 --> 00:12:19.519 that. They didn't know exactly

NOTE Confidence: 0.9576709

00:12:19.519 --> 00:12:20.959 what was going on. And

NOTE Confidence: 0.9576709

00:12:20.959 --> 00:12:22.820 this was in the journal

NOTE Confidence: 0.9576709

00:12:22.880 --> 00:12:23.380 of

NOTE Confidence: 0.9335338

00:12:23.774 --> 00:12:25.054 Gebir Stalin, which I think

NOTE Confidence: 0.9335338

00:12:25.054 --> 00:12:25.795 is gynecology,

NOTE Confidence: 0.89551234

00:12:26.735 --> 00:12:28.274 maybe pregnancy, and gynecology.

NOTE Confidence: 0.9953284

00:12:28.654 --> 00:12:29.875 You can see that gynecology

NOTE Confidence: 0.9953284

00:12:30.095 --> 00:12:31.535 still exists as a word

NOTE Confidence: 0.9953284

00:12:31.535 --> 00:12:32.894 here in this journal. So

NOTE Confidence: 0.9953284

00:12:32.894 --> 00:12:34.014 this is really the first

NOTE Confidence: 0.9953284

00:12:34.014 --> 00:12:35.295 publication I was able to

NOTE Confidence: 0.9953284

00:12:35.295 --> 00:12:36.510 find of it. There was

NOTE Confidence: 0.9953284

00:12:36.510 --> 00:12:37.170 a fantastic

NOTE Confidence: 0.975595

00:12:37.710 --> 00:12:39.650 volume in nineteen twenty one

NOTE Confidence: 0.975595

00:12:39.870 --> 00:12:41.950 that looked at twelve hundred

NOTE Confidence: 0.975595

00:12:41.950 --> 00:12:42.990 cases as part of the

NOTE Confidence: 0.975595

00:12:42.990 --> 00:12:44.050 Carnegie collection.

NOTE Confidence: 0.9618191

00:12:44.990 --> 00:12:46.190 Look at these pictures. These

NOTE Confidence: 0.9618191

00:12:46.190 --> 00:12:47.470 are exactly the same as

NOTE Confidence: 0.9618191

00:12:47.470 --> 00:12:48.990 the tropholastic inclusions I just

NOTE Confidence: 0.9618191

00:12:48.990 --> 00:12:50.590 showed you back in nineteen

NOTE Confidence: 0.9618191

00:12:50.590 --> 00:12:51.955 twenty one. And what I

NOTE Confidence: 0.9618191

00:12:51.955 --> 00:12:53.895 like especially about this

NOTE Confidence: 0.96844655

00:12:54.595 --> 00:12:56.675 reference is that they describe

NOTE Confidence: 0.96844655

00:12:56.675 --> 00:12:58.855 the exact characteristics of tropholass

NOTE Confidence: 0.96844655

00:12:58.915 --> 00:13:01.075 inclusions here. They say there

NOTE Confidence: 0.96844655

00:13:01.075 --> 00:13:02.515 are numerous points of the

NOTE Confidence: 0.96844655

00:13:02.515 --> 00:13:03.895 syncytium that invade.

NOTE Confidence: 0.9759399

00:13:04.529 --> 00:13:06.050 They are lined by two

NOTE Confidence: 0.9759399

00:13:06.050 --> 00:13:07.490 layers of cells, just like

NOTE Confidence: 0.9759399

00:13:07.490 --> 00:13:08.690 I showed you, which are

NOTE Confidence: 0.9759399

00:13:08.690 --> 00:13:10.290 often filled with dense masses

NOTE Confidence: 0.9759399

00:13:10.290 --> 00:13:12.050 of small round cells. So,

NOTE Confidence: 0.9759399

00:13:12.050 --> 00:13:13.110 that is the definition

NOTE Confidence: 0.99540216

00:13:13.730 --> 00:13:15.429 of a trophoblast inclusion.

NOTE Confidence: 0.9936224

00:13:16.050 --> 00:13:17.809 Now, the word trophoblast inclusion

NOTE Confidence: 0.9936224

00:13:17.809 --> 00:13:19.089 was actually coined in this

NOTE Confidence: 0.9936224

00:13:19.089 --> 00:13:20.505 paper in nineteen sixty four

NOTE Confidence: 0.9936224

00:13:20.505 --> 00:13:21.885 by Boyd and Hamilton.

NOTE Confidence: 0.9723694

00:13:22.505 --> 00:13:23.705 The title of their paper

NOTE Confidence: 0.9723694

00:13:23.705 --> 00:13:25.005 was Stromal trophoblastic

NOTE Confidence: 0.97718143

00:13:25.545 --> 00:13:26.985 buds. And we do not

NOTE Confidence: 0.97718143

00:13:26.985 --> 00:13:28.265 write this way anymore, but

NOTE Confidence: 0.97718143

00:13:28.265 --> 00:13:29.725 I love that they describe

NOTE Confidence: 0.98359823

00:13:30.265 --> 00:13:31.705 the creation of these in

NOTE Confidence: 0.98359823

00:13:31.705 --> 00:13:33.065 this paper, and then they

NOTE Confidence: 0.98359823

00:13:33.065 --> 00:13:34.665 have a little asterisk under

NOTE Confidence: 0.98359823

00:13:34.665 --> 00:13:36.600 their title, stromal trophoblastic

NOTE Confidence: 0.9555218

00:13:36.980 --> 00:13:38.420 buds, and they say, The

NOTE Confidence: 0.9555218

00:13:38.420 --> 00:13:39.940 question of a suitable term

NOTE Confidence: 0.9555218

00:13:39.940 --> 00:13:41.080 for the trophoblastic

NOTE Confidence: 0.9993366

00:13:41.620 --> 00:13:42.120 inclusions

NOTE Confidence: 0.9984473

00:13:42.580 --> 00:13:44.120 has given us some concern.

NOTE Confidence: 0.9686962

00:13:44.500 --> 00:13:46.840 So their parenthetic comment here,

NOTE Confidence: 0.9686962

00:13:46.900 --> 00:13:48.260 in fact, has become the

NOTE Confidence: 0.9686962

00:13:48.260 --> 00:13:49.380 name of these things and

NOTE Confidence: 0.9686962

00:13:49.380 --> 00:13:50.900 it started in nineteen sixty

NOTE Confidence: 0.9686962

00:13:50.900 --> 00:13:52.635 four. As I pointed out

NOTE Confidence: 0.9686962

00:13:52.635 --> 00:13:54.154 before, they did something cool

NOTE Confidence: 0.9686962

00:13:54.154 --> 00:13:55.595 in this paper. They did

NOTE Confidence: 0.9686962

00:13:55.595 --> 00:13:56.735 three d reconstruction.

NOTE Confidence: 0.9468754

00:13:57.355 --> 00:13:58.875 They did serous sections of

NOTE Confidence: 0.9468754

00:13:58.875 --> 00:14:00.735 multiple sections of these placentas

NOTE Confidence: 0.9468754

00:14:00.795 --> 00:14:02.175 with the trophoblast inclusions.

NOTE Confidence: 0.96832067

00:14:03.035 --> 00:14:04.315 And in the top left,

NOTE Confidence: 0.96832067

00:14:04.315 --> 00:14:05.275 you can see the three

NOTE Confidence: 0.96832067

00:14:05.275 --> 00:14:06.015 d reconstruction,

NOTE Confidence: 0.9917359

00:14:06.635 --> 00:14:08.520 and it points out again

NOTE Confidence: 0.9917359

00:14:08.740 --> 00:14:10.500 that these inclusions are nothing

NOTE Confidence: 0.9917359

00:14:10.500 --> 00:14:11.640 more than invaginations

NOTE Confidence: 0.977842

00:14:12.020 --> 00:14:13.460 from the surface with sort

NOTE Confidence: 0.977842

00:14:13.460 --> 00:14:15.220 of bulbous ends to them.

NOTE Confidence: 0.977842

00:14:15.220 --> 00:14:16.420 And if you cut through

NOTE Confidence: 0.977842

00:14:16.420 --> 00:14:18.100 the bulb, it appears as

NOTE Confidence: 0.977842

00:14:18.100 --> 00:14:19.400 a trophoblast inclusion.

NOTE Confidence: 0.9636076

00:14:20.345 --> 00:14:21.785 Okay. So that's the history

NOTE Confidence: 0.9636076

00:14:21.785 --> 00:14:23.464 of it. What causes it?

NOTE Confidence: 0.9636076

00:14:23.464 --> 00:14:24.904 And this will this will

NOTE Confidence: 0.9636076

00:14:24.904 --> 00:14:26.345 actually answer a little bit

NOTE Confidence: 0.9636076

00:14:26.345 --> 00:14:28.685 Hugh Taylor's insightful question there.

NOTE Confidence: 0.9866666

00:14:29.144 --> 00:14:30.425 It wasn't a plant. I

NOTE Confidence: 0.9866666

00:14:30.425 --> 00:14:31.464 did not ask him to

NOTE Confidence: 0.9866666

00:14:31.464 --> 00:14:33.245 ask that question, just FYI.

NOTE Confidence: 0.965357

00:14:33.865 --> 00:14:35.324 So what causes these trophoblast

NOTE Confidence: 0.965357

00:14:35.430 --> 00:14:37.270 inclusions? Well, to understand what

NOTE Confidence: 0.965357

00:14:37.270 --> 00:14:38.630 causes them, you have to

NOTE Confidence: 0.965357

00:14:38.630 --> 00:14:39.830 go back to the basic

NOTE Confidence: 0.965357

00:14:39.830 --> 00:14:41.050 structure of the placenta.

NOTE Confidence: 0.9245413

00:14:41.830 --> 00:14:42.870 And I have mentioned a

NOTE Confidence: 0.9245413

00:14:42.870 --> 00:14:43.990 couple times, and I'm going

NOTE Confidence: 0.9245413

00:14:43.990 --> 00:14:45.430 to highlight this, that the

NOTE Confidence: 0.9245413

00:14:45.430 --> 00:14:45.930 placenta,

NOTE Confidence: 0.96714133

00:14:46.310 --> 00:14:47.589 the villi are lined by

NOTE Confidence: 0.96714133

00:14:47.589 --> 00:14:49.029 two layers of cells, the

NOTE Confidence: 0.96714133

00:14:49.029 --> 00:14:49.529 cytotrophoblast,

NOTE Confidence: 0.9824257

00:14:50.070 --> 00:14:51.555 the stem cell, and the

NOTE Confidence: 0.9824257

00:14:51.555 --> 00:14:52.055 syncytiotrophoblast.

NOTE Confidence: 0.9537384

00:14:52.995 --> 00:14:54.275 And I was lucky enough

NOTE Confidence: 0.9537384

00:14:54.275 --> 00:14:55.415 when I did my postdoctoral

NOTE Confidence: 0.9537384

00:14:55.635 --> 00:14:57.315 research fellowship at University of

NOTE Confidence: 0.9537384

00:14:57.315 --> 00:14:59.395 Pennsylvania with Jerry Straus, just

NOTE Confidence: 0.9537384

00:14:59.395 --> 00:15:00.135 by serendipity,

NOTE Confidence: 0.9569107

00:15:00.595 --> 00:15:01.635 I assure you it was

NOTE Confidence: 0.9569107

00:15:01.635 --> 00:15:02.295 by accident,

NOTE Confidence: 0.9873367

00:15:02.755 --> 00:15:04.790 I discovered the relationship of

NOTE Confidence: 0.9873367

00:15:04.790 --> 00:15:05.450 the cytotrophoblasts

NOTE Confidence: 0.9461956

00:15:05.830 --> 00:15:07.430 and the syncytial trophoblasts by

NOTE Confidence: 0.9461956

00:15:07.430 --> 00:15:08.550 looking at these cells in

NOTE Confidence: 0.9461956

00:15:08.550 --> 00:15:10.070 culture, and what I saw

NOTE Confidence: 0.9461956

00:15:10.070 --> 00:15:11.750 on time lapse movies is

NOTE Confidence: 0.9461956

00:15:11.750 --> 00:15:13.130 that these single cytotrophoblasts

NOTE Confidence: 0.98743105

00:15:13.670 --> 00:15:14.950 in culture over a period

NOTE Confidence: 0.98743105

00:15:14.950 --> 00:15:15.765 of four days

NOTE Confidence: 0.995015

00:15:16.325 --> 00:15:17.545 moved, aggregated,

NOTE Confidence: 0.9767423

00:15:18.005 --> 00:15:19.525 the membranes broke down, and

NOTE Confidence: 0.9767423

00:15:19.525 --> 00:15:20.585 they formed syncytia.

NOTE Confidence: 0.99729127

00:15:21.125 --> 00:15:22.805 Up to that point, people

NOTE Confidence: 0.99729127

00:15:22.805 --> 00:15:24.885 thought that syncytial trophoblasts were

NOTE Confidence: 0.99729127

00:15:24.885 --> 00:15:26.245 formed by a process called

NOTE Confidence: 0.99729127

00:15:26.245 --> 00:15:26.745 endoreduplication,

NOTE Confidence: 0.9766545

00:15:27.685 --> 00:15:29.385 which means that the nuclei

NOTE Confidence: 0.9766545

00:15:29.685 --> 00:15:31.230 divide and divide, but we

NOTE Confidence: 0.9766545

00:15:31.310 --> 00:15:32.910 showed in this paper that

NOTE Confidence: 0.9766545

00:15:32.910 --> 00:15:34.670 they actually form by fusion

NOTE Confidence: 0.9766545

00:15:34.670 --> 00:15:35.490 of the cytotrophoblasts.

NOTE Confidence: 0.9979346

00:15:36.350 --> 00:15:37.949 Taking that insight into the

NOTE Confidence: 0.9979346

00:15:37.949 --> 00:15:39.870 placenta itself, we can now

NOTE Confidence: 0.9979346

00:15:39.870 --> 00:15:41.389 look at the bilayer and

NOTE Confidence: 0.9979346

00:15:41.389 --> 00:15:42.990 answer Hugh Taylor's question in

NOTE Confidence: 0.9979346

00:15:42.990 --> 00:15:44.370 more scientific detail.

NOTE Confidence: 0.97591937

00:15:44.834 --> 00:15:45.574 These cytotrophoblasts

NOTE Confidence: 0.97524375

00:15:46.035 --> 00:15:47.475 have two choices in life.

NOTE Confidence: 0.97524375

00:15:47.475 --> 00:15:48.615 They either proliferate

NOTE Confidence: 0.92882717

00:15:49.074 --> 00:15:50.134 or if they differentiate,

NOTE Confidence: 0.9746231

00:15:50.595 --> 00:15:52.134 they fuse with the overlying

NOTE Confidence: 0.9746231

00:15:52.274 --> 00:15:54.774 layer. And there's kinetic constants

NOTE Confidence: 0.9746231

00:15:54.915 --> 00:15:56.694 for proliferation and fusion.

NOTE Confidence: 0.95850855

00:15:57.220 --> 00:15:58.580 And depending, again, as I

NOTE Confidence: 0.95850855

00:15:58.580 --> 00:16:00.100 said before, but now highlighted

NOTE Confidence: 0.95850855

00:16:00.100 --> 00:16:01.080 in this publication,

NOTE Confidence: 0.99435693

00:16:01.860 --> 00:16:03.000 if the proliferation

NOTE Confidence: 0.9871135

00:16:03.460 --> 00:16:04.600 rate of the cytotrophoblast

NOTE Confidence: 0.9871986

00:16:05.060 --> 00:16:06.740 is greater than two times

NOTE Confidence: 0.9871986

00:16:06.740 --> 00:16:08.660 the fusion rate, it bends

NOTE Confidence: 0.9871986

00:16:08.660 --> 00:16:10.520 inward. That forms the invagination.

NOTE Confidence: 0.99934095

00:16:11.505 --> 00:16:13.185 If the fusion rate is

NOTE Confidence: 0.99934095

00:16:13.185 --> 00:16:14.645 greater than the

NOTE Confidence: 0.9887498

00:16:15.265 --> 00:16:18.485 proliferation rate, it branches outward.

NOTE Confidence: 0.9887498

00:16:18.625 --> 00:16:20.165 That's called branching morphogenesis.

NOTE Confidence: 0.98285145

00:16:20.785 --> 00:16:21.665 And this is how the

NOTE Confidence: 0.98285145

00:16:21.665 --> 00:16:23.285 placenta normally forms.

NOTE Confidence: 0.95185065

00:16:23.720 --> 00:16:25.260 If the rate is exactly

NOTE Confidence: 0.95185065

00:16:25.400 --> 00:16:27.560 equal where proliferation equals two

NOTE Confidence: 0.95185065

00:16:27.560 --> 00:16:29.080 times the fusion rate, there's

NOTE Confidence: 0.95185065

00:16:29.080 --> 00:16:30.060 just a lengthening

NOTE Confidence: 0.9937536

00:16:30.360 --> 00:16:32.440 of the bilayer. So these

NOTE Confidence: 0.9937536

00:16:32.440 --> 00:16:34.060 are the three kinetic constants

NOTE Confidence: 0.9981618

00:16:34.360 --> 00:16:35.720 that explain the whole growth

NOTE Confidence: 0.9981618

00:16:35.720 --> 00:16:36.540 of the placenta.

NOTE Confidence: 0.90213984

00:16:37.415 --> 00:16:39.435 So up until this point,

NOTE Confidence: 0.9810134

00:16:39.814 --> 00:16:41.735 what I basically had seen

NOTE Confidence: 0.9810134

00:16:41.735 --> 00:16:43.735 clinically through my clinical experience

NOTE Confidence: 0.9810134

00:16:43.735 --> 00:16:45.274 is that trophoblast inclusions

NOTE Confidence: 0.98132277

00:16:45.814 --> 00:16:48.154 are associated with pregnancy losses

NOTE Confidence: 0.98132277

00:16:48.214 --> 00:16:49.254 and, as I'll show you

NOTE Confidence: 0.98132277

00:16:49.254 --> 00:16:50.615 in a few minutes, very

NOTE Confidence: 0.98132277

00:16:50.615 --> 00:16:51.435 small placentas.

NOTE Confidence: 0.99336797

00:16:52.055 --> 00:16:52.555 So

NOTE Confidence: 0.9601238

00:16:52.860 --> 00:16:53.900 here is a paper that

NOTE Confidence: 0.9601238

00:16:53.900 --> 00:16:55.600 we recently published in Reproductive

NOTE Confidence: 0.9601238

00:16:55.820 --> 00:16:57.839 Sciences in twenty twenty three

NOTE Confidence: 0.9841615

00:16:58.140 --> 00:16:59.500 where we looked at the

NOTE Confidence: 0.9841615

00:16:59.500 --> 00:17:02.300 causes of pregnancy losses between

NOTE Confidence: 0.9841615

00:17:02.300 --> 00:17:03.900 six weeks and forty three

NOTE Confidence: 0.9841615

00:17:03.900 --> 00:17:05.900 weeks. I've created what's called

NOTE Confidence: 0.9841615

00:17:05.900 --> 00:17:07.660 a density plot here of

NOTE Confidence: 0.9841615

00:17:07.660 --> 00:17:08.240 the different

NOTE Confidence: 0.9858915

00:17:08.565 --> 00:17:10.325 pathologies that were identified in

NOTE Confidence: 0.9858915

00:17:10.325 --> 00:17:11.865 these losses. There were almost

NOTE Confidence: 0.9858915

00:17:12.005 --> 00:17:13.764 thirteen hundred of them. And

NOTE Confidence: 0.9858915

00:17:13.764 --> 00:17:14.725 you can see that the

NOTE Confidence: 0.9858915

00:17:14.725 --> 00:17:15.225 dominant

NOTE Confidence: 0.98975664

00:17:15.764 --> 00:17:17.845 cause of pregnancy loss in

NOTE Confidence: 0.98975664

00:17:17.845 --> 00:17:19.524 the first and certainly second

NOTE Confidence: 0.98975664

00:17:19.524 --> 00:17:20.024 trimester

NOTE Confidence: 0.9694474

00:17:20.609 --> 00:17:22.450 are dysmorphic or associated with

NOTE Confidence: 0.9694474

00:17:22.450 --> 00:17:24.850 dysmorphic chorionic villi, which we've

NOTE Confidence: 0.9694474

00:17:24.850 --> 00:17:26.630 interpreted are due to genetic

NOTE Confidence: 0.9694474

00:17:26.690 --> 00:17:28.070 abnormalities. Of course,

NOTE Confidence: 0.98809445

00:17:28.530 --> 00:17:29.970 the reason I'm so excited

NOTE Confidence: 0.98809445

00:17:29.970 --> 00:17:31.970 about the gPRPL study is

NOTE Confidence: 0.98809445

00:17:31.970 --> 00:17:33.190 I would like to validate

NOTE Confidence: 0.98809445

00:17:33.285 --> 00:17:34.725 this. This is currently a

NOTE Confidence: 0.98809445

00:17:34.725 --> 00:17:35.225 hypothesis

NOTE Confidence: 0.9838943

00:17:35.525 --> 00:17:37.525 based on the visualization of

NOTE Confidence: 0.9838943

00:17:37.525 --> 00:17:39.285 trophoblast inclusions. So this is

NOTE Confidence: 0.9838943

00:17:39.285 --> 00:17:39.945 the entire

NOTE Confidence: 0.8598696

00:17:40.725 --> 00:17:41.225 population.

NOTE Confidence: 0.98982215

00:17:41.685 --> 00:17:42.645 I can show you the

NOTE Confidence: 0.98982215

00:17:42.645 --> 00:17:44.005 same data in a pie

NOTE Confidence: 0.98982215

00:17:44.005 --> 00:17:45.445 chart, and you can see

NOTE Confidence: 0.98982215

00:17:45.445 --> 00:17:47.000 that about seventy one percent

NOTE Confidence: 0.98982215

00:17:47.000 --> 00:17:48.679 of all pregnancy losses have

NOTE Confidence: 0.98982215

00:17:48.679 --> 00:17:49.820 trophoblast inclusions,

NOTE Confidence: 0.9833693

00:17:50.119 --> 00:17:51.080 and then there are some

NOTE Confidence: 0.9833693

00:17:51.080 --> 00:17:52.520 other causes which are here

NOTE Confidence: 0.9833693

00:17:52.520 --> 00:17:53.960 in these other pieces of

NOTE Confidence: 0.9833693

00:17:53.960 --> 00:17:54.619 the pie.

NOTE Confidence: 0.99605703

00:17:55.080 --> 00:17:56.359 If we focus just on

NOTE Confidence: 0.99605703

00:17:56.359 --> 00:17:56.859 miscarriages,

NOTE Confidence: 0.9843426

00:17:57.320 --> 00:17:59.419 again, defined as pregnancy losses

NOTE Confidence: 0.9843426

00:17:59.480 --> 00:18:01.045 less than twenty weeks, and

NOTE Confidence: 0.9843426

00:18:01.045 --> 00:18:02.165 look at the pie chart

NOTE Confidence: 0.9843426

00:18:02.165 --> 00:18:04.005 for that, eighty six percent

NOTE Confidence: 0.9843426

00:18:04.005 --> 00:18:06.105 are associated with trophoblast inclusions.

NOTE Confidence: 0.9856288

00:18:07.845 --> 00:18:09.465 And if we look at

NOTE Confidence: 0.9856288

00:18:09.605 --> 00:18:11.845 stillbirths now, greater than twenty

NOTE Confidence: 0.9856288

00:18:11.845 --> 00:18:13.385 weeks, twenty weeks and greater,

NOTE Confidence: 0.99051696

00:18:13.685 --> 00:18:14.805 here is what the pie

NOTE Confidence: 0.99051696

00:18:14.805 --> 00:18:16.185 chart looks like here.

NOTE Confidence: 0.9666268

00:18:16.580 --> 00:18:18.180 Now the causes are slightly

NOTE Confidence: 0.9666268

00:18:18.180 --> 00:18:20.020 different. Genetics is still quite

NOTE Confidence: 0.9666268

00:18:20.020 --> 00:18:21.140 a bit at thirty percent,

NOTE Confidence: 0.9666268

00:18:21.140 --> 00:18:22.359 but small placentas

NOTE Confidence: 0.90870476

00:18:22.740 --> 00:18:24.500 are thirty three percent and

NOTE Confidence: 0.90870476

00:18:24.500 --> 00:18:26.340 cord accidents are about fifteen

NOTE Confidence: 0.90870476

00:18:26.340 --> 00:18:26.840 percent.

NOTE Confidence: 0.98549783

00:18:27.220 --> 00:18:28.820 But what's interesting is that

NOTE Confidence: 0.98549783

00:18:28.820 --> 00:18:29.940 if you look at just

NOTE Confidence: 0.98549783

00:18:29.940 --> 00:18:31.494 the third trimester, and this

NOTE Confidence: 0.98549783

00:18:31.494 --> 00:18:32.215 is where I think we

NOTE Confidence: 0.98549783

00:18:32.215 --> 00:18:33.734 should, from now on, have

NOTE Confidence: 0.98549783

00:18:33.734 --> 00:18:35.335 the division of miscarriages and

NOTE Confidence: 0.98549783

00:18:35.335 --> 00:18:35.835 stillbirths,

NOTE Confidence: 0.98604745

00:18:36.215 --> 00:18:37.255 this is a U shaped

NOTE Confidence: 0.98604745

00:18:37.255 --> 00:18:38.215 curve and this is the

NOTE Confidence: 0.98604745

00:18:38.215 --> 00:18:39.734 inflection point right at the

NOTE Confidence: 0.98604745

00:18:39.734 --> 00:18:41.035 end of the second trimester.

NOTE Confidence: 0.9922658

00:18:41.415 --> 00:18:43.015 I believe that all first

NOTE Confidence: 0.9922658

00:18:43.015 --> 00:18:45.175 trimester and second trimester losses

NOTE Confidence: 0.9922658

00:18:45.175 --> 00:18:46.990 really are very similar, and

NOTE Confidence: 0.9922658

00:18:46.990 --> 00:18:48.750 it's the third trimester that

NOTE Confidence: 0.9922658

00:18:48.750 --> 00:18:50.450 diverge and are quite different.

NOTE Confidence: 0.9922658

00:18:50.670 --> 00:18:51.869 But what's interesting when you

NOTE Confidence: 0.9922658

00:18:51.869 --> 00:18:52.830 look at the pie chart

NOTE Confidence: 0.9922658

00:18:52.830 --> 00:18:54.109 of that, now you can

NOTE Confidence: 0.9922658

00:18:54.109 --> 00:18:55.809 see that thirty six percent

NOTE Confidence: 0.9922658

00:18:55.950 --> 00:18:57.309 of stillbirths are due to

NOTE Confidence: 0.9922658

00:18:57.309 --> 00:18:59.630 small placentas, only sixteen percent

NOTE Confidence: 0.9922658

00:18:59.630 --> 00:19:00.130 genetics,

NOTE Confidence: 0.99671185

00:19:00.565 --> 00:19:02.085 and twenty one percent cord

NOTE Confidence: 0.99671185

00:19:02.085 --> 00:19:03.845 accidents. However, when you look

NOTE Confidence: 0.99671185

00:19:03.845 --> 00:19:05.285 at the causes for small

NOTE Confidence: 0.99671185

00:19:05.285 --> 00:19:05.785 placentas,

NOTE Confidence: 0.999711

00:19:06.325 --> 00:19:07.845 the majority of the small

NOTE Confidence: 0.999711

00:19:07.845 --> 00:19:09.545 placentas are due to genetic

NOTE Confidence: 0.999711

00:19:09.605 --> 00:19:10.105 abnormalities.

NOTE Confidence: 0.9622608

00:19:10.805 --> 00:19:12.085 Okay, well, this has all

NOTE Confidence: 0.9622608

00:19:12.085 --> 00:19:13.545 have been just an introduction

NOTE Confidence: 0.9622608

00:19:13.765 --> 00:19:14.645 to go back to our

NOTE Confidence: 0.9622608

00:19:14.645 --> 00:19:16.340 patient here, which is setting

NOTE Confidence: 0.9622608

00:19:16.340 --> 00:19:17.640 up this whole discussion.

NOTE Confidence: 0.9706897

00:19:17.940 --> 00:19:19.220 So, let's look at NH

NOTE Confidence: 0.9706897

00:19:19.220 --> 00:19:20.420 again and see what we

NOTE Confidence: 0.9706897

00:19:20.420 --> 00:19:20.920 found.

NOTE Confidence: 0.9766603

00:19:21.460 --> 00:19:23.220 I found an average of

NOTE Confidence: 0.9766603

00:19:23.220 --> 00:19:25.480 one point seven trophoblast inclusions

NOTE Confidence: 0.9766603

00:19:25.619 --> 00:19:27.140 per slide in her thirty

NOTE Confidence: 0.9766603

00:19:27.140 --> 00:19:28.615 two week loss. And you

NOTE Confidence: 0.9766603

00:19:28.615 --> 00:19:29.895 may say, That's not really

NOTE Confidence: 0.9766603

00:19:29.895 --> 00:19:31.414 that much, but normal is

NOTE Confidence: 0.9766603

00:19:31.414 --> 00:19:33.095 zero point one. So this

NOTE Confidence: 0.9766603

00:19:33.095 --> 00:19:35.335 is seventeen times normal, and

NOTE Confidence: 0.9766603

00:19:35.335 --> 00:19:36.934 this is a classic example

NOTE Confidence: 0.9766603

00:19:36.934 --> 00:19:38.615 of a small placenta associated

NOTE Confidence: 0.9766603

00:19:38.615 --> 00:19:39.994 with trophoblast inclusions.

NOTE Confidence: 0.9790867

00:19:40.534 --> 00:19:42.215 Her sixteen week loss had

NOTE Confidence: 0.9790867

00:19:42.215 --> 00:19:43.914 three point five per slide

NOTE Confidence: 0.9790867

00:19:44.109 --> 00:19:45.889 or thirty five times normal,

NOTE Confidence: 0.96947634

00:19:46.190 --> 00:19:47.730 and her twelve week loss

NOTE Confidence: 0.96947634

00:19:47.950 --> 00:19:49.789 had ninety times normal the

NOTE Confidence: 0.96947634

00:19:49.789 --> 00:19:51.330 number of trophoblast inclusions.

NOTE Confidence: 0.9555116

00:19:51.950 --> 00:19:53.389 So as you can see,

NOTE Confidence: 0.9555116

00:19:53.389 --> 00:19:54.429 there seems to be a

NOTE Confidence: 0.9555116

00:19:54.429 --> 00:19:56.109 dose response curve. And if

NOTE Confidence: 0.9555116

00:19:56.109 --> 00:19:57.465 we plot out on the

NOTE Confidence: 0.9555116

00:19:57.465 --> 00:19:58.905 y axis the number of

NOTE Confidence: 0.9555116

00:19:58.905 --> 00:20:00.905 trophoblasts inclusions per slide is

NOTE Confidence: 0.9555116

00:20:00.905 --> 00:20:01.405 some

NOTE Confidence: 0.9869834

00:20:01.785 --> 00:20:04.025 metric of how many there

NOTE Confidence: 0.9869834

00:20:04.025 --> 00:20:05.385 are, you can see that

NOTE Confidence: 0.9869834

00:20:05.385 --> 00:20:07.005 there is a crude relationship

NOTE Confidence: 0.97227454

00:20:07.465 --> 00:20:09.065 between the severity of the

NOTE Confidence: 0.97227454

00:20:09.065 --> 00:20:10.984 genetic problem with tetraploidy, for

NOTE Confidence: 0.97227454

00:20:10.984 --> 00:20:12.750 example, having the most, then

NOTE Confidence: 0.97227454

00:20:12.750 --> 00:20:15.710 triploidy less, trisomies less, pregnancy

NOTE Confidence: 0.97227454

00:20:15.710 --> 00:20:17.890 losses with apparently normal karyotypes,

NOTE Confidence: 0.9398383

00:20:18.350 --> 00:20:20.290 and finally, stillbirths, and then

NOTE Confidence: 0.89323187

00:20:20.750 --> 00:20:22.369 at the extreme left,

NOTE Confidence: 0.8802388

00:20:23.150 --> 00:20:24.050 normal pregnancies.

NOTE Confidence: 0.9760765

00:20:25.565 --> 00:20:27.265 So if we then plot

NOTE Confidence: 0.9760765

00:20:27.325 --> 00:20:28.525 the three losses of the

NOTE Confidence: 0.9760765

00:20:28.525 --> 00:20:29.965 patient NH on this, you

NOTE Confidence: 0.9760765

00:20:29.965 --> 00:20:30.925 can see it fits this

NOTE Confidence: 0.9760765

00:20:30.925 --> 00:20:32.525 curve very well. Here's her

NOTE Confidence: 0.9760765

00:20:32.525 --> 00:20:33.725 twelve week loss that had

NOTE Confidence: 0.9760765

00:20:33.725 --> 00:20:35.105 the most number of inclusions,

NOTE Confidence: 0.99041504

00:20:35.405 --> 00:20:37.244 her sixteen week had less,

NOTE Confidence: 0.99041504

00:20:37.244 --> 00:20:38.525 and her thirty two week

NOTE Confidence: 0.99041504

00:20:38.525 --> 00:20:39.744 loss had the least.

NOTE Confidence: 0.9968646

00:20:40.109 --> 00:20:42.530 Basically, the more trophoblast inclusions,

NOTE Confidence: 0.9968646

00:20:42.670 --> 00:20:44.609 the earlier the pregnancy loss.

NOTE Confidence: 0.9708558

00:20:45.230 --> 00:20:46.830 So, frankly, for many years,

NOTE Confidence: 0.9708558

00:20:46.830 --> 00:20:48.430 I'm a practical person. I

NOTE Confidence: 0.9708558

00:20:48.430 --> 00:20:50.030 simply used the presence of

NOTE Confidence: 0.9708558

00:20:50.030 --> 00:20:51.790 trophoblast inclusions as a check

NOTE Confidence: 0.9708558

00:20:51.790 --> 00:20:52.609 engine light

NOTE Confidence: 0.9149677

00:20:52.934 --> 00:20:54.375 but really didn't do much

NOTE Confidence: 0.9149677

00:20:54.375 --> 00:20:55.494 else with it. Can I

NOTE Confidence: 0.9149677

00:20:55.494 --> 00:20:55.894 can I,

NOTE Confidence: 0.93421656

00:20:56.855 --> 00:20:58.294 comment on one thing? We

NOTE Confidence: 0.93421656

00:20:58.294 --> 00:20:59.894 just had one case two

NOTE Confidence: 0.93421656

00:20:59.894 --> 00:21:01.514 weeks ago in NICU,

NOTE Confidence: 0.862158

00:21:01.975 --> 00:21:03.274 has a triple priority,

NOTE Confidence: 0.8607259

00:21:03.654 --> 00:21:05.095 and it's a twenty six

NOTE Confidence: 0.8607259

00:21:05.095 --> 00:21:06.315 week end of delivery.

NOTE Confidence: 0.9142739

00:21:06.810 --> 00:21:07.690 So you might look at

NOTE Confidence: 0.9142739

00:21:07.690 --> 00:21:08.990 that back in that percentage.

NOTE Confidence: 0.9362682

00:21:09.450 --> 00:21:11.150 If that's possible, it's somewhere.

NOTE Confidence: 0.9606369

00:21:11.690 --> 00:21:12.890 I'm sure it's somewhere. And

NOTE Confidence: 0.9606369

00:21:12.890 --> 00:21:14.330 do me a favor, Yong

NOTE Confidence: 0.9606369

00:21:14.330 --> 00:21:15.530 Wei. I appreciate. Just send

NOTE Confidence: 0.9606369

00:21:15.530 --> 00:21:16.730 me an email with the

NOTE Confidence: 0.9606369

00:21:16.730 --> 00:21:18.010 MR number, and I will

NOTE Confidence: 0.9606369

00:21:18.010 --> 00:21:19.605 definitely look at that. That's

NOTE Confidence: 0.9606369

00:21:19.605 --> 00:21:21.445 fantastic. Yeah. I appreciate. And

NOTE Confidence: 0.9606369

00:21:21.445 --> 00:21:23.205 for anybody listening, wherever you

NOTE Confidence: 0.9606369

00:21:23.205 --> 00:21:24.165 are in the country, if

NOTE Confidence: 0.9606369

00:21:24.165 --> 00:21:25.765 you have pregnancy losses that

NOTE Confidence: 0.9606369

00:21:25.765 --> 00:21:27.285 you do not know why

NOTE Confidence: 0.9606369

00:21:27.285 --> 00:21:28.725 they've occurred or patients with

NOTE Confidence: 0.9606369

00:21:28.725 --> 00:21:30.565 multiple losses, and especially if

NOTE Confidence: 0.9606369

00:21:30.565 --> 00:21:31.765 they're stillbirths and can't be

NOTE Confidence: 0.9606369

00:21:31.765 --> 00:21:32.665 part of GPRPL,

NOTE Confidence: 0.98248553

00:21:33.320 --> 00:21:34.440 I would be very happy

NOTE Confidence: 0.98248553

00:21:34.440 --> 00:21:35.880 to look at them. So,

NOTE Confidence: 0.98248553

00:21:35.880 --> 00:21:37.400 frankly, I was minding my

NOTE Confidence: 0.98248553

00:21:37.400 --> 00:21:38.760 own business at this point

NOTE Confidence: 0.98248553

00:21:38.760 --> 00:21:40.280 just looking at pregnancy losses

NOTE Confidence: 0.98248553

00:21:40.280 --> 00:21:41.340 and being a clinician

NOTE Confidence: 0.93959105

00:21:41.640 --> 00:21:42.840 and using the presence of

NOTE Confidence: 0.93959105

00:21:42.840 --> 00:21:44.359 triple s inclusions as this

NOTE Confidence: 0.93959105

00:21:44.359 --> 00:21:44.859 marker

NOTE Confidence: 0.9169121

00:21:45.320 --> 00:21:46.220 when, unfortunately,

NOTE Confidence: 0.97980267

00:21:46.600 --> 00:21:48.300 in nineteen ninety eight, Wakefield

NOTE Confidence: 0.97980267

00:21:48.440 --> 00:21:50.195 publishes now, in my opinion,

NOTE Confidence: 0.97980267

00:21:50.255 --> 00:21:50.755 infamous,

NOTE Confidence: 0.9150663

00:21:51.294 --> 00:21:53.075 unfortunately, recently resurrected

NOTE Confidence: 0.9645996

00:21:53.534 --> 00:21:55.215 paper here showing that the

NOTE Confidence: 0.9645996

00:21:55.215 --> 00:21:56.975 MMR vaccine was, in his

NOTE Confidence: 0.9645996

00:21:56.975 --> 00:21:58.434 opinion, the cause of autism.

NOTE Confidence: 0.9990645

00:21:59.135 --> 00:22:01.054 And because of that, people

NOTE Confidence: 0.9990645

00:22:01.054 --> 00:22:01.955 started believing

NOTE Confidence: 0.9993765

00:22:02.335 --> 00:22:03.315 that their children's

NOTE Confidence: 0.96773595

00:22:04.130 --> 00:22:05.250 autism was due to the

NOTE Confidence: 0.96773595

00:22:05.250 --> 00:22:06.769 MMR vaccines that they were

NOTE Confidence: 0.96773595

00:22:06.769 --> 00:22:08.210 given when these children were

NOTE Confidence: 0.96773595

00:22:08.210 --> 00:22:10.389 younger. And so not surprisingly

NOTE Confidence: 0.96773595

00:22:10.450 --> 00:22:11.809 in this country, these people

NOTE Confidence: 0.96773595

00:22:11.809 --> 00:22:13.730 started suing their doctors, their

NOTE Confidence: 0.96773595

00:22:13.730 --> 00:22:15.585 pediatricians, and vaccine makers.

NOTE Confidence: 0.9823734

00:22:16.625 --> 00:22:17.505 You know, as we all

NOTE Confidence: 0.9823734

00:22:17.505 --> 00:22:19.345 know, the Wakefield paper was

NOTE Confidence: 0.9823734

00:22:19.345 --> 00:22:20.705 retracted and shown to be

NOTE Confidence: 0.9823734

00:22:20.705 --> 00:22:22.784 completely fraudulent, but that hasn't

NOTE Confidence: 0.9823734

00:22:22.784 --> 00:22:24.544 stopped people from still believing

NOTE Confidence: 0.9823734

00:22:24.544 --> 00:22:26.645 this. Well, at this point,

NOTE Confidence: 0.9823734

00:22:26.945 --> 00:22:27.984 and one of the things

NOTE Confidence: 0.9823734

00:22:27.984 --> 00:22:29.265 I do in my life,

NOTE Confidence: 0.9823734

00:22:29.265 --> 00:22:29.970 because I'm one of the

NOTE Confidence: 0.9823734

00:22:29.970 --> 00:22:31.170 few people who looks at

NOTE Confidence: 0.9823734

00:22:31.170 --> 00:22:31.670 placentas,

NOTE Confidence: 0.9985013

00:22:32.210 --> 00:22:33.650 is that I look at

NOTE Confidence: 0.9985013

00:22:33.650 --> 00:22:34.150 cases

NOTE Confidence: 0.9236731

00:22:35.010 --> 00:22:36.230 of legal cases

NOTE Confidence: 0.9749452

00:22:36.770 --> 00:22:38.450 that either plaintiff's attorneys or

NOTE Confidence: 0.9749452

00:22:38.450 --> 00:22:39.350 defense attorneys,

NOTE Confidence: 0.99010026

00:22:39.650 --> 00:22:41.250 have to try to help

NOTE Confidence: 0.99010026

00:22:41.250 --> 00:22:42.450 them figure out why there

NOTE Confidence: 0.99010026

00:22:42.450 --> 00:22:44.130 was a pregnancy complication or

NOTE Confidence: 0.99010026

00:22:44.130 --> 00:22:45.505 loss. And in this case,

NOTE Confidence: 0.99010026

00:22:45.505 --> 00:22:46.305 I was asked by a

NOTE Confidence: 0.99010026

00:22:46.305 --> 00:22:47.525 number of defense attorneys

NOTE Confidence: 0.9634325

00:22:47.905 --> 00:22:48.965 to look at the placentas

NOTE Confidence: 0.9634325

00:22:49.025 --> 00:22:50.705 from these children and see,

NOTE Confidence: 0.9634325

00:22:50.705 --> 00:22:52.244 could there be another explanation

NOTE Confidence: 0.9634325

00:22:52.305 --> 00:22:54.405 for this children's autism?

NOTE Confidence: 0.99957275

00:22:54.945 --> 00:22:55.445 Well,

NOTE Confidence: 0.9978774

00:22:55.744 --> 00:22:57.265 I will just quote Louis

NOTE Confidence: 0.9978774

00:22:57.265 --> 00:22:57.765 Pasteur,

NOTE Confidence: 0.9037347

00:22:58.380 --> 00:23:00.720 December seventh eighteen fifty four,

NOTE Confidence: 0.9037347

00:23:00.940 --> 00:23:02.400 In the fields of observation,

NOTE Confidence: 0.9734965

00:23:02.700 --> 00:23:04.619 chance favors only the prepared

NOTE Confidence: 0.9734965

00:23:04.619 --> 00:23:06.460 mind. And luckily, because I

NOTE Confidence: 0.9734965

00:23:06.460 --> 00:23:07.900 have been doing for years

NOTE Confidence: 0.9734965

00:23:07.900 --> 00:23:09.740 work on pregnancy losses and

NOTE Confidence: 0.9734965

00:23:09.740 --> 00:23:11.280 looking at trophoblast inclusions,

NOTE Confidence: 0.95543414

00:23:11.705 --> 00:23:12.665 when I looked at these

NOTE Confidence: 0.95543414

00:23:12.665 --> 00:23:14.685 placentas of children with autism,

NOTE Confidence: 0.9816773

00:23:15.225 --> 00:23:17.225 I found trophoblast inclusions, and

NOTE Confidence: 0.9816773

00:23:17.225 --> 00:23:18.205 I said to myself,

NOTE Confidence: 0.9598883

00:23:18.505 --> 00:23:19.785 wow, I think this might

NOTE Confidence: 0.9598883

00:23:19.785 --> 00:23:21.385 be, in fact, genetic and

NOTE Confidence: 0.9598883

00:23:21.385 --> 00:23:22.685 not due to the MMR

NOTE Confidence: 0.9598883

00:23:22.744 --> 00:23:23.244 vaccine,

NOTE Confidence: 0.9348046

00:23:23.545 --> 00:23:25.140 which at the time was

NOTE Confidence: 0.9348046

00:23:25.140 --> 00:23:26.900 novel because really people did

NOTE Confidence: 0.9348046

00:23:26.900 --> 00:23:27.859 believe it was due to

NOTE Confidence: 0.9348046

00:23:27.859 --> 00:23:29.080 the MMR vaccine.

NOTE Confidence: 0.9748239

00:23:29.460 --> 00:23:30.420 So what do you do

NOTE Confidence: 0.9748239

00:23:30.420 --> 00:23:31.619 when you're posed with this,

NOTE Confidence: 0.9748239

00:23:32.020 --> 00:23:33.540 problem? Well, you do research.

NOTE Confidence: 0.9748239

00:23:33.540 --> 00:23:34.820 So the first thing we

NOTE Confidence: 0.9748239

00:23:34.820 --> 00:23:36.420 did is a retrospective study,

NOTE Confidence: 0.9748239

00:23:36.420 --> 00:23:37.619 which we published in two

NOTE Confidence: 0.9748239

00:23:37.619 --> 00:23:39.285 thousand and seven, and although

NOTE Confidence: 0.9748239

00:23:39.285 --> 00:23:40.585 it was a small study,

NOTE Confidence: 0.9748239

00:23:40.725 --> 00:23:42.185 we did show a statistically

NOTE Confidence: 0.9748239

00:23:42.405 --> 00:23:44.485 significant difference between placentas from

NOTE Confidence: 0.9748239

00:23:44.485 --> 00:23:46.025 children with proven autism

NOTE Confidence: 0.9925741

00:23:46.565 --> 00:23:48.005 and those that were controls

NOTE Confidence: 0.9925741

00:23:48.005 --> 00:23:50.085 in this particular study. Well,

NOTE Confidence: 0.9925741

00:23:50.085 --> 00:23:52.265 retrospective studies are flawed,

NOTE Confidence: 0.98714584

00:23:52.725 --> 00:23:54.490 and obviously, I wanted to

NOTE Confidence: 0.98714584

00:23:54.490 --> 00:23:56.410 do a prospective study, but

NOTE Confidence: 0.98714584

00:23:56.410 --> 00:23:57.710 it's very challenging

NOTE Confidence: 0.99940515

00:23:58.170 --> 00:23:59.790 to do a prospective study

NOTE Confidence: 0.99940515

00:23:59.930 --> 00:24:01.230 of children with autism.

NOTE Confidence: 0.96861166

00:24:01.850 --> 00:24:03.630 Their incidence is two percent

NOTE Confidence: 0.96861166

00:24:03.770 --> 00:24:05.369 at most, and it's very

NOTE Confidence: 0.96861166

00:24:05.369 --> 00:24:07.055 hard to follow these kids

NOTE Confidence: 0.96861166

00:24:07.055 --> 00:24:08.175 and then get all the

NOTE Confidence: 0.96861166

00:24:08.175 --> 00:24:09.695 placentas, and not all placentas

NOTE Confidence: 0.96861166

00:24:09.695 --> 00:24:10.755 are sent to pathology.

NOTE Confidence: 0.9678157

00:24:11.135 --> 00:24:12.175 So I was really, for

NOTE Confidence: 0.9678157

00:24:12.175 --> 00:24:13.615 four years, in a complete

NOTE Confidence: 0.9678157

00:24:13.615 --> 00:24:15.615 stagnation with this project. But

NOTE Confidence: 0.9678157

00:24:15.615 --> 00:24:17.055 luckily, on the front page

NOTE Confidence: 0.9678157

00:24:17.055 --> 00:24:18.095 of The New York Times

NOTE Confidence: 0.9678157

00:24:18.095 --> 00:24:19.455 in November first of twenty

NOTE Confidence: 0.9678157

00:24:19.455 --> 00:24:19.955 ten,

NOTE Confidence: 0.90520906

00:24:20.630 --> 00:24:21.910 in the left top corner

NOTE Confidence: 0.90520906

00:24:21.910 --> 00:24:23.350 was an article that was

NOTE Confidence: 0.90520906

00:24:23.350 --> 00:24:24.470 titled At the Age of

NOTE Confidence: 0.90520906

00:24:24.470 --> 00:24:25.670 Pick a Boo in Therapy

NOTE Confidence: 0.90520906

00:24:25.670 --> 00:24:26.650 to Fight Autism.

NOTE Confidence: 0.97910273

00:24:27.110 --> 00:24:28.730 And this was a article

NOTE Confidence: 0.97910273

00:24:28.870 --> 00:24:29.770 about a study

NOTE Confidence: 0.9898207

00:24:30.550 --> 00:24:32.090 that was looking at placentas

NOTE Confidence: 0.9898207

00:24:32.310 --> 00:24:33.690 of children with autism.

NOTE Confidence: 0.98071355

00:24:34.105 --> 00:24:35.304 And I will challenge you

NOTE Confidence: 0.98071355

00:24:35.304 --> 00:24:36.904 to find another article on

NOTE Confidence: 0.98071355

00:24:36.904 --> 00:24:37.784 the front page of the

NOTE Confidence: 0.98071355

00:24:37.784 --> 00:24:38.744 New York Times that has

NOTE Confidence: 0.98071355

00:24:38.744 --> 00:24:40.105 the word placenta in it.

NOTE Confidence: 0.98071355

00:24:40.105 --> 00:24:41.404 It is a rare occurrence.

NOTE Confidence: 0.97288084

00:24:42.264 --> 00:24:43.544 So I was very struck

NOTE Confidence: 0.97288084

00:24:43.544 --> 00:24:44.764 by this, and I immediately

NOTE Confidence: 0.97288084

00:24:44.904 --> 00:24:46.904 contacted the people at the

NOTE Confidence: 0.97288084

00:24:46.904 --> 00:24:49.085 MIND Institute at UC Davis,

NOTE Confidence: 0.97288084

00:24:49.330 --> 00:24:51.090 and I said, look, I

NOTE Confidence: 0.97288084

00:24:51.090 --> 00:24:52.130 would love to look at

NOTE Confidence: 0.97288084

00:24:52.130 --> 00:24:53.650 the placentas that you are

NOTE Confidence: 0.97288084

00:24:53.650 --> 00:24:55.190 collecting for your reasons.

NOTE Confidence: 0.98857933

00:24:55.810 --> 00:24:57.330 As an aside, they believe

NOTE Confidence: 0.98857933

00:24:57.330 --> 00:24:58.850 the cause of autism were

NOTE Confidence: 0.98857933

00:24:58.850 --> 00:24:59.350 pesticides

NOTE Confidence: 0.9588116

00:24:59.730 --> 00:25:00.710 in the Sacramento,

NOTE Confidence: 0.99636316

00:25:01.090 --> 00:25:01.750 you know,

NOTE Confidence: 0.95442957

00:25:02.095 --> 00:25:03.315 area of California.

NOTE Confidence: 0.98044205

00:25:03.855 --> 00:25:05.295 I didn't really, you know,

NOTE Confidence: 0.98044205

00:25:05.295 --> 00:25:06.655 acknowledge that. It didn't matter

NOTE Confidence: 0.98044205

00:25:06.655 --> 00:25:07.615 to me what they thought

NOTE Confidence: 0.98044205

00:25:07.615 --> 00:25:08.575 the cause was. I just

NOTE Confidence: 0.98044205

00:25:08.575 --> 00:25:09.375 wanted to look at the

NOTE Confidence: 0.98044205

00:25:09.375 --> 00:25:09.875 placentas,

NOTE Confidence: 0.9396625

00:25:10.335 --> 00:25:12.415 and they begrudgingly eventually did

NOTE Confidence: 0.9396625

00:25:12.415 --> 00:25:13.535 send me two hundred and

NOTE Confidence: 0.9396625

00:25:13.535 --> 00:25:14.515 seventeen cases.

NOTE Confidence: 0.99966323

00:25:15.119 --> 00:25:15.859 And there

NOTE Confidence: 0.98008347

00:25:16.320 --> 00:25:17.859 were a hundred and seventeen

NOTE Confidence: 0.98916054

00:25:18.160 --> 00:25:19.700 kids at risk for autism

NOTE Confidence: 0.98916054

00:25:19.760 --> 00:25:21.520 and high risk families and

NOTE Confidence: 0.98916054

00:25:21.520 --> 00:25:22.580 a hundred controls.

NOTE Confidence: 0.9621141

00:25:23.119 --> 00:25:24.480 And without going through the

NOTE Confidence: 0.9621141

00:25:24.480 --> 00:25:25.840 details of this paper here

NOTE Confidence: 0.9621141

00:25:25.840 --> 00:25:26.820 because of time,

NOTE Confidence: 0.98639363

00:25:27.165 --> 00:25:28.765 this just graphically shows you

NOTE Confidence: 0.98639363

00:25:28.765 --> 00:25:30.205 that there were far more

NOTE Confidence: 0.98639363

00:25:30.205 --> 00:25:31.965 trophoblast inclusions in the at

NOTE Confidence: 0.98639363

00:25:31.965 --> 00:25:33.585 risk population on the left

NOTE Confidence: 0.98639363

00:25:33.725 --> 00:25:35.085 compared to the controls. And

NOTE Confidence: 0.98639363

00:25:35.085 --> 00:25:35.744 in fact,

NOTE Confidence: 0.9786125

00:25:36.045 --> 00:25:38.045 no control placenta had more

NOTE Confidence: 0.9786125

00:25:38.045 --> 00:25:39.885 than an average of point

NOTE Confidence: 0.9786125

00:25:39.885 --> 00:25:42.150 five trophoblast inclusions per slide.

NOTE Confidence: 0.9786125

00:25:42.150 --> 00:25:43.430 You might remember the numbers

NOTE Confidence: 0.9786125

00:25:43.430 --> 00:25:44.490 I showed you before.

NOTE Confidence: 0.9923971

00:25:44.790 --> 00:25:45.910 And this is the plot

NOTE Confidence: 0.9923971

00:25:45.910 --> 00:25:47.270 of those cases on the

NOTE Confidence: 0.9923971

00:25:47.270 --> 00:25:48.390 same graph I showed you

NOTE Confidence: 0.9923971

00:25:48.390 --> 00:25:49.990 before. Here are the normal

NOTE Confidence: 0.9923971

00:25:49.990 --> 00:25:51.350 placentas with an average of

NOTE Confidence: 0.9923971

00:25:51.350 --> 00:25:52.390 point one, and that's where

NOTE Confidence: 0.9923971

00:25:52.390 --> 00:25:53.690 we get that data from.

NOTE Confidence: 0.9923971

00:25:53.830 --> 00:25:55.210 And the at risk placentas

NOTE Confidence: 0.9923971

00:25:55.270 --> 00:25:56.550 from these families had an

NOTE Confidence: 0.9923971

00:25:56.550 --> 00:25:58.090 average of point five. So

NOTE Confidence: 0.9923971

00:25:58.095 --> 00:25:59.615 it's not that much more,

NOTE Confidence: 0.9923971

00:25:59.615 --> 00:26:00.895 but remember, if you have

NOTE Confidence: 0.9923971

00:26:00.895 --> 00:26:02.434 too many trophoblast inclusions,

NOTE Confidence: 0.97523475

00:26:02.975 --> 00:26:04.655 you're a pregnancy loss. So

NOTE Confidence: 0.97523475

00:26:04.655 --> 00:26:06.015 these are children that were

NOTE Confidence: 0.97523475

00:26:06.015 --> 00:26:07.934 born but had something going

NOTE Confidence: 0.97523475

00:26:07.934 --> 00:26:08.835 on with them.

NOTE Confidence: 0.9623449

00:26:09.375 --> 00:26:11.054 Well, my question for myself

NOTE Confidence: 0.9623449

00:26:11.054 --> 00:26:12.480 was, and again, I'm gonna

NOTE Confidence: 0.9623449

00:26:12.480 --> 00:26:13.600 go back to Hugh Taylor's

NOTE Confidence: 0.9623449

00:26:13.600 --> 00:26:15.359 question, why are the tissues

NOTE Confidence: 0.9623449

00:26:15.359 --> 00:26:16.400 bending one way or the

NOTE Confidence: 0.9623449

00:26:16.400 --> 00:26:16.900 other?

NOTE Confidence: 0.93628764

00:26:17.359 --> 00:26:18.960 Why is bending of the

NOTE Confidence: 0.93628764

00:26:18.960 --> 00:26:20.340 placenta and invaginations

NOTE Confidence: 0.99029094

00:26:20.880 --> 00:26:22.640 related to autism? So I

NOTE Confidence: 0.99029094

00:26:22.640 --> 00:26:23.540 started investigating

NOTE Confidence: 0.949587

00:26:24.125 --> 00:26:25.005 autism a little bit, what

NOTE Confidence: 0.949587

00:26:25.005 --> 00:26:26.125 was known about the brains

NOTE Confidence: 0.949587

00:26:26.125 --> 00:26:27.345 of children with autism.

NOTE Confidence: 0.98254436

00:26:27.725 --> 00:26:29.244 And what's interesting among many

NOTE Confidence: 0.98254436

00:26:29.244 --> 00:26:30.845 things of children with autism,

NOTE Confidence: 0.98254436

00:26:30.845 --> 00:26:31.744 people with autism,

NOTE Confidence: 0.95057964

00:26:32.125 --> 00:26:33.725 their brains are actually folded

NOTE Confidence: 0.95057964

00:26:33.725 --> 00:26:35.025 more at a microscopic

NOTE Confidence: 0.9612517

00:26:35.405 --> 00:26:36.445 level. Here is,

NOTE Confidence: 0.94993824

00:26:36.845 --> 00:26:38.785 Margaret Bowman's work at Harvard

NOTE Confidence: 0.94993824

00:26:38.990 --> 00:26:39.950 who has shown at a

NOTE Confidence: 0.94993824

00:26:39.950 --> 00:26:41.630 microscopic level, the brains of

NOTE Confidence: 0.94993824

00:26:41.630 --> 00:26:43.310 these children are folded more,

NOTE Confidence: 0.94993824

00:26:43.310 --> 00:26:45.070 and here's an MRI study

NOTE Confidence: 0.94993824

00:26:45.070 --> 00:26:46.510 on the left showing that

NOTE Confidence: 0.94993824

00:26:46.510 --> 00:26:47.250 the macroscopic

NOTE Confidence: 0.99281424

00:26:47.710 --> 00:26:48.910 level of the brains are

NOTE Confidence: 0.99281424

00:26:48.910 --> 00:26:50.910 also folded more. So my

NOTE Confidence: 0.99281424

00:26:50.910 --> 00:26:52.270 thought was, well, maybe this

NOTE Confidence: 0.99281424

00:26:52.270 --> 00:26:53.490 has to do with folding.

NOTE Confidence: 0.9956214

00:26:53.790 --> 00:26:55.125 Maybe that's really the source

NOTE Confidence: 0.9956214

00:26:55.125 --> 00:26:56.565 of the problem here. And

NOTE Confidence: 0.9956214

00:26:56.565 --> 00:26:57.765 then I was very struck

NOTE Confidence: 0.9956214

00:26:57.765 --> 00:26:58.885 by this article that was

NOTE Confidence: 0.9956214

00:26:58.885 --> 00:27:00.265 published in twenty thirteen.

NOTE Confidence: 0.9996701

00:27:00.645 --> 00:27:01.785 This was a pulmonologist

NOTE Confidence: 0.99733347

00:27:02.165 --> 00:27:03.605 who was seeing children with

NOTE Confidence: 0.99733347

00:27:03.605 --> 00:27:05.945 autism that had pulmonary problems.

NOTE Confidence: 0.99733347

00:27:06.165 --> 00:27:07.385 She was doing bronchoscopies

NOTE Confidence: 0.9545299

00:27:07.925 --> 00:27:09.545 looking at the bronchial tree,

NOTE Confidence: 0.9545299

00:27:09.600 --> 00:27:10.740 and what she showed

NOTE Confidence: 0.9644804

00:27:11.119 --> 00:27:12.320 on the left, the normal

NOTE Confidence: 0.9644804

00:27:12.320 --> 00:27:14.100 bronchial tree looks like this.

NOTE Confidence: 0.99848217

00:27:14.400 --> 00:27:16.160 The bronchial trees of children

NOTE Confidence: 0.99848217

00:27:16.160 --> 00:27:16.980 with autism

NOTE Confidence: 0.9975139

00:27:17.280 --> 00:27:19.780 were more folded, more branched,

NOTE Confidence: 0.9992836

00:27:20.320 --> 00:27:21.780 different than the normals.

NOTE Confidence: 0.9442309

00:27:22.445 --> 00:27:23.965 So the question is, is

NOTE Confidence: 0.9442309

00:27:23.965 --> 00:27:25.744 this, in fact, a global

NOTE Confidence: 0.9442309

00:27:25.885 --> 00:27:26.945 increase of folding,

NOTE Confidence: 0.9978584

00:27:27.244 --> 00:27:28.365 and why would there be

NOTE Confidence: 0.9978584

00:27:28.365 --> 00:27:29.885 any advantage? Why would you

NOTE Confidence: 0.9978584

00:27:29.885 --> 00:27:31.345 want to have more folding?

NOTE Confidence: 0.98234284

00:27:31.885 --> 00:27:33.265 And I would like to

NOTE Confidence: 0.98234284

00:27:33.484 --> 00:27:35.025 propose, this is a hypothesis,

NOTE Confidence: 0.98234284

00:27:35.244 --> 00:27:36.285 it's hard to prove these

NOTE Confidence: 0.98234284

00:27:36.285 --> 00:27:38.010 things, that there actually is

NOTE Confidence: 0.98234284

00:27:38.010 --> 00:27:39.450 a benefit to folding, and

NOTE Confidence: 0.98234284

00:27:39.450 --> 00:27:40.410 I'd like to share that

NOTE Confidence: 0.98234284

00:27:40.410 --> 00:27:41.950 with you in a hypothesis

NOTE Confidence: 0.98234284

00:27:42.170 --> 00:27:43.690 I call the pelvis skull

NOTE Confidence: 0.98234284

00:27:43.690 --> 00:27:44.750 conflict hypothesis.

NOTE Confidence: 0.9733561

00:27:45.370 --> 00:27:46.570 I presented this in twenty

NOTE Confidence: 0.9733561

00:27:46.570 --> 00:27:48.410 fifteen at the Institute Society

NOTE Confidence: 0.9733561

00:27:48.410 --> 00:27:49.790 for Evolutionary Medicine.

NOTE Confidence: 0.97780627

00:27:50.330 --> 00:27:51.770 And what I was pointing

NOTE Confidence: 0.97780627

00:27:51.770 --> 00:27:54.034 out is that our babies'

NOTE Confidence: 0.9934829

00:27:54.654 --> 00:27:55.635 skull sizes,

NOTE Confidence: 0.9606499

00:27:56.174 --> 00:27:57.075 head sizes,

NOTE Confidence: 0.9668029

00:27:57.695 --> 00:27:59.695 are the largest compared to

NOTE Confidence: 0.9668029

00:27:59.695 --> 00:28:01.534 any other primate compared to

NOTE Confidence: 0.9668029

00:28:01.534 --> 00:28:03.375 the pelvic outflow. So here

NOTE Confidence: 0.9668029

00:28:03.375 --> 00:28:04.335 we are in the lower

NOTE Confidence: 0.9668029

00:28:04.335 --> 00:28:05.875 right corner, Homo sapiens,

NOTE Confidence: 0.9993058

00:28:06.910 --> 00:28:08.290 and we have maximized

NOTE Confidence: 0.9997186

00:28:08.830 --> 00:28:10.210 the amount of space

NOTE Confidence: 0.99616724

00:28:10.510 --> 00:28:12.350 that we can pack brain

NOTE Confidence: 0.99616724

00:28:12.350 --> 00:28:14.190 into. In other words, we

NOTE Confidence: 0.99616724

00:28:14.190 --> 00:28:15.869 cannot make the heads of

NOTE Confidence: 0.99616724

00:28:15.869 --> 00:28:17.710 babies any bigger. The only

NOTE Confidence: 0.99616724

00:28:17.710 --> 00:28:19.330 way to get increased intelligence

NOTE Confidence: 0.99216133

00:28:19.630 --> 00:28:20.830 is to actually have more

NOTE Confidence: 0.99216133

00:28:20.830 --> 00:28:22.405 folding. And as it is

NOTE Confidence: 0.99216133

00:28:22.405 --> 00:28:22.905 now,

NOTE Confidence: 0.9985959

00:28:23.285 --> 00:28:24.645 our brains are the most

NOTE Confidence: 0.9985959

00:28:24.645 --> 00:28:26.744 folded primate brain that exists.

NOTE Confidence: 0.86170125

00:28:27.285 --> 00:28:28.505 So, again,

NOTE Confidence: 0.9792879

00:28:28.805 --> 00:28:30.325 why is that? Well, because

NOTE Confidence: 0.9792879

00:28:30.325 --> 00:28:31.845 I think there's more computing

NOTE Confidence: 0.9792879

00:28:31.845 --> 00:28:33.205 power when you have more

NOTE Confidence: 0.9792879

00:28:33.205 --> 00:28:35.140 folded brains, and there's evidence

NOTE Confidence: 0.9792879

00:28:35.140 --> 00:28:36.760 of that. There are genetic

NOTE Confidence: 0.9792879

00:28:36.820 --> 00:28:38.840 conditions that lead to complete

NOTE Confidence: 0.9792879

00:28:38.980 --> 00:28:40.600 severe developmental disabilities

NOTE Confidence: 0.9634545

00:28:41.700 --> 00:28:43.780 and brain development intelligence, and

NOTE Confidence: 0.9634545

00:28:43.780 --> 00:28:45.620 they're associated with poorly folded

NOTE Confidence: 0.9634545

00:28:45.620 --> 00:28:46.980 brains. You can think of

NOTE Confidence: 0.9634545

00:28:46.980 --> 00:28:48.680 the normal population here.

NOTE Confidence: 0.9649188

00:28:49.174 --> 00:28:51.174 Autism seems to have increased

NOTE Confidence: 0.9649188

00:28:51.174 --> 00:28:51.674 folding,

NOTE Confidence: 0.9993725

00:28:52.294 --> 00:28:53.815 and we know that there

NOTE Confidence: 0.9993725

00:28:53.815 --> 00:28:55.755 is an association of intelligence

NOTE Confidence: 0.9993725

00:28:55.895 --> 00:28:56.635 with autism.

NOTE Confidence: 0.9764365

00:28:57.015 --> 00:28:58.215 I'm not gonna name some

NOTE Confidence: 0.9764365

00:28:58.215 --> 00:28:59.335 names, but just think of

NOTE Confidence: 0.9764365

00:28:59.335 --> 00:29:00.775 some carmakers that you know

NOTE Confidence: 0.9764365

00:29:00.775 --> 00:29:01.835 who are very intelligent

NOTE Confidence: 0.979236

00:29:02.375 --> 00:29:03.515 and are on the spectrum,

NOTE Confidence: 0.979236

00:29:03.799 --> 00:29:05.000 and maybe people who are

NOTE Confidence: 0.979236

00:29:05.000 --> 00:29:06.600 computer people and engineers and

NOTE Confidence: 0.979236

00:29:06.600 --> 00:29:07.799 work at MIT and other

NOTE Confidence: 0.979236

00:29:07.799 --> 00:29:09.240 things like that. So I

NOTE Confidence: 0.979236

00:29:09.240 --> 00:29:11.179 think that the evolutionary pressure

NOTE Confidence: 0.979236

00:29:11.240 --> 00:29:12.760 that we're looking at here

NOTE Confidence: 0.979236

00:29:12.760 --> 00:29:14.380 is for increased intelligence

NOTE Confidence: 0.9257063

00:29:15.000 --> 00:29:16.539 that when it's too severe

NOTE Confidence: 0.9257063

00:29:16.760 --> 00:29:18.039 leads to something that we

NOTE Confidence: 0.9257063

00:29:18.039 --> 00:29:18.940 call autism.

NOTE Confidence: 0.9968742

00:29:20.165 --> 00:29:22.085 Now, in evolution, there is

NOTE Confidence: 0.9968742

00:29:22.085 --> 00:29:23.525 no free lunch. There is

NOTE Confidence: 0.9968742

00:29:23.525 --> 00:29:24.825 something called antagonistic

NOTE Confidence: 0.86649823

00:29:25.205 --> 00:29:25.705 pleiotropy,

NOTE Confidence: 0.99383956

00:29:26.405 --> 00:29:27.945 and I call this collateral

NOTE Confidence: 0.99383956

00:29:28.085 --> 00:29:30.105 damage, basically. That's my interpretation

NOTE Confidence: 0.99383956

00:29:30.325 --> 00:29:31.924 of this. If there are

NOTE Confidence: 0.99383956

00:29:31.924 --> 00:29:33.285 genes that are trying to

NOTE Confidence: 0.99383956

00:29:33.285 --> 00:29:34.505 make us more intelligent,

NOTE Confidence: 0.98986745

00:29:35.080 --> 00:29:36.780 there might be some collateral

NOTE Confidence: 0.98986745

00:29:36.920 --> 00:29:38.360 damage to that and negative

NOTE Confidence: 0.98986745

00:29:38.360 --> 00:29:38.860 impact.

NOTE Confidence: 0.97797817

00:29:39.160 --> 00:29:39.960 And one of the things

NOTE Confidence: 0.97797817

00:29:39.960 --> 00:29:41.740 that I was really struggling

NOTE Confidence: 0.97797817

00:29:41.800 --> 00:29:42.920 with during the years of

NOTE Confidence: 0.97797817

00:29:42.920 --> 00:29:44.680 doing this research is how

NOTE Confidence: 0.97797817

00:29:44.680 --> 00:29:45.660 is it possible

NOTE Confidence: 0.96067894

00:29:45.960 --> 00:29:47.800 that trophoblast inclusions in the

NOTE Confidence: 0.96067894

00:29:47.800 --> 00:29:48.885 placenta could

NOTE Confidence: 0.981174

00:29:49.925 --> 00:29:51.465 lead to pregnancy loss?

NOTE Confidence: 0.9717812

00:29:51.925 --> 00:29:53.125 It didn't seem logical to

NOTE Confidence: 0.9717812

00:29:53.125 --> 00:29:54.485 me. And even when there

NOTE Confidence: 0.9717812

00:29:54.485 --> 00:29:56.005 are hundred times the number

NOTE Confidence: 0.9717812

00:29:56.005 --> 00:29:57.605 of trophoblast inclusions that there

NOTE Confidence: 0.9717812

00:29:57.605 --> 00:29:58.645 should be, and this is

NOTE Confidence: 0.9717812

00:29:58.645 --> 00:29:59.765 from a paper where I

NOTE Confidence: 0.9717812

00:29:59.765 --> 00:30:01.620 actually plotted out on a

NOTE Confidence: 0.9717812

00:30:01.620 --> 00:30:02.820 map form on the right

NOTE Confidence: 0.9717812

00:30:02.820 --> 00:30:04.920 here where the trophalescent inclusions

NOTE Confidence: 0.9717812

00:30:04.980 --> 00:30:06.180 are, you can see that

NOTE Confidence: 0.9717812

00:30:06.180 --> 00:30:07.380 there are very, very few

NOTE Confidence: 0.9717812

00:30:07.380 --> 00:30:08.920 of them in the whole

NOTE Confidence: 0.9717812

00:30:09.060 --> 00:30:09.560 spectrum

NOTE Confidence: 0.95289016

00:30:10.020 --> 00:30:10.920 of the placenta.

NOTE Confidence: 0.9134515

00:30:11.300 --> 00:30:12.440 So in my opinion,

NOTE Confidence: 0.9196298

00:30:12.900 --> 00:30:14.745 these inclusions are not affecting

NOTE Confidence: 0.9196298

00:30:14.825 --> 00:30:15.865 affecting the function of the

NOTE Confidence: 0.9196298

00:30:15.865 --> 00:30:16.925 placenta whatsoever.

NOTE Confidence: 0.8459513

00:30:17.305 --> 00:30:18.125 So the question

NOTE Confidence: 0.9682531

00:30:18.745 --> 00:30:20.425 is, what organ could be

NOTE Confidence: 0.9682531

00:30:20.425 --> 00:30:20.925 deleteriously

NOTE Confidence: 0.9840184

00:30:21.305 --> 00:30:23.705 affected by increased folding? And

NOTE Confidence: 0.9840184

00:30:23.705 --> 00:30:24.985 I'd like to do a

NOTE Confidence: 0.9840184

00:30:24.985 --> 00:30:26.905 thought experiment with you, kind

NOTE Confidence: 0.9840184

00:30:26.905 --> 00:30:28.665 of a knockout experiment with

NOTE Confidence: 0.9840184

00:30:28.665 --> 00:30:29.705 the whole body at this

NOTE Confidence: 0.9840184

00:30:29.705 --> 00:30:31.309 point. So if you imagine

NOTE Confidence: 0.9840184

00:30:31.370 --> 00:30:32.809 a fetus and we are

NOTE Confidence: 0.9840184

00:30:32.809 --> 00:30:34.090 in the uterus, we're not

NOTE Confidence: 0.9840184

00:30:34.090 --> 00:30:35.370 outside the uterus, but if

NOTE Confidence: 0.9840184

00:30:35.370 --> 00:30:36.409 you imagine we're in the

NOTE Confidence: 0.9840184

00:30:36.409 --> 00:30:38.250 uterus, my question is, what

NOTE Confidence: 0.9840184

00:30:38.250 --> 00:30:40.570 is necessary for life, not

NOTE Confidence: 0.9840184

00:30:40.570 --> 00:30:42.510 high quality life, just existence?

NOTE Confidence: 0.96263695

00:30:43.174 --> 00:30:44.535 Well, you can remove the

NOTE Confidence: 0.96263695

00:30:44.535 --> 00:30:46.135 entire GI tract without any

NOTE Confidence: 0.96263695

00:30:46.135 --> 00:30:47.255 problem in a fetus. You

NOTE Confidence: 0.96263695

00:30:47.255 --> 00:30:48.135 don't need it. You have

NOTE Confidence: 0.96263695

00:30:48.135 --> 00:30:48.794 the placenta.

NOTE Confidence: 0.99285007

00:30:49.174 --> 00:30:50.775 You can remove the entire

NOTE Confidence: 0.99285007

00:30:50.775 --> 00:30:52.315 GU system. It's unnecessary.

NOTE Confidence: 0.98946357

00:30:53.015 --> 00:30:54.215 You can remove the liver,

NOTE Confidence: 0.98946357

00:30:54.215 --> 00:30:55.495 the spleen, and the pancreas.

NOTE Confidence: 0.98946357

00:30:55.495 --> 00:30:56.475 They're not necessary.

NOTE Confidence: 0.87702507

00:30:56.840 --> 00:30:58.120 You can remove the lungs.

NOTE Confidence: 0.87702507

00:30:58.120 --> 00:31:00.360 Unfortunately, they're very clear clinical,

NOTE Confidence: 0.87702507

00:31:00.360 --> 00:31:01.980 Potter syndrome as an example,

NOTE Confidence: 0.9806014

00:31:02.280 --> 00:31:03.640 where the lungs don't ever

NOTE Confidence: 0.9806014

00:31:03.640 --> 00:31:05.080 develop, and you can exist

NOTE Confidence: 0.9806014

00:31:05.080 --> 00:31:05.900 in the uterus.

NOTE Confidence: 0.96528435

00:31:06.280 --> 00:31:07.880 Unfortunately, you don't need the

NOTE Confidence: 0.96528435

00:31:07.880 --> 00:31:08.840 brain or head, and we

NOTE Confidence: 0.96528435

00:31:08.840 --> 00:31:10.300 know lots of people who

NOTE Confidence: 0.96528435

00:31:10.360 --> 00:31:11.800 are ex vivo that is

NOTE Confidence: 0.96528435

00:31:11.800 --> 00:31:12.674 the case, and that's not

NOTE Confidence: 0.96528435

00:31:12.674 --> 00:31:13.815 necessary either.

NOTE Confidence: 0.9155167

00:31:14.115 --> 00:31:15.634 So sorry, I couldn't help

NOTE Confidence: 0.9155167

00:31:15.634 --> 00:31:16.134 it.

NOTE Confidence: 0.97080904

00:31:16.595 --> 00:31:18.034 But there is one last

NOTE Confidence: 0.97080904

00:31:18.034 --> 00:31:20.674 organ that is completely necessary

NOTE Confidence: 0.97080904

00:31:20.674 --> 00:31:21.634 for life, and that is

NOTE Confidence: 0.97080904

00:31:21.634 --> 00:31:23.255 the heart. And in fact,

NOTE Confidence: 0.97080904

00:31:23.394 --> 00:31:25.255 the heart is the only

NOTE Confidence: 0.97080904

00:31:25.554 --> 00:31:27.890 essential organ. Now, what's interesting

NOTE Confidence: 0.97080904

00:31:27.890 --> 00:31:29.250 about the heart is that

NOTE Confidence: 0.97080904

00:31:29.250 --> 00:31:30.789 it's formed by complex

NOTE Confidence: 0.9907278

00:31:31.169 --> 00:31:31.669 folding.

NOTE Confidence: 0.95952755

00:31:33.010 --> 00:31:34.210 That is how the heart

NOTE Confidence: 0.95952755

00:31:34.210 --> 00:31:34.950 is made.

NOTE Confidence: 0.99701726

00:31:35.809 --> 00:31:37.510 And it is very susceptible

NOTE Confidence: 0.981778

00:31:37.970 --> 00:31:40.070 to abnormal folding, and abnormal

NOTE Confidence: 0.981778

00:31:40.130 --> 00:31:42.630 folding leads to pregnancy loss.

NOTE Confidence: 0.98959875

00:31:43.385 --> 00:31:45.304 Here's just an example of

NOTE Confidence: 0.98959875

00:31:45.304 --> 00:31:47.065 an amazing paper that looked

NOTE Confidence: 0.98959875

00:31:47.065 --> 00:31:48.684 at the details of embryonic

NOTE Confidence: 0.98959875

00:31:48.825 --> 00:31:50.424 heart development between three point

NOTE Confidence: 0.98959875

00:31:50.424 --> 00:31:51.544 five and eight weeks of

NOTE Confidence: 0.98959875

00:31:51.544 --> 00:31:52.524 human development.

NOTE Confidence: 0.9843976

00:31:52.985 --> 00:31:54.024 And this is just one

NOTE Confidence: 0.9843976

00:31:54.024 --> 00:31:55.465 of their figures. It's too

NOTE Confidence: 0.9843976

00:31:55.465 --> 00:31:56.664 complex for me to even

NOTE Confidence: 0.9843976

00:31:56.664 --> 00:31:57.705 follow what was going on

NOTE Confidence: 0.9843976

00:31:57.705 --> 00:31:59.220 with these hearts. But in

NOTE Confidence: 0.9843976

00:31:59.220 --> 00:32:00.820 general, what I gained from

NOTE Confidence: 0.9843976

00:32:00.820 --> 00:32:02.100 this paper is that it's

NOTE Confidence: 0.9843976

00:32:02.100 --> 00:32:03.320 extremely complex,

NOTE Confidence: 0.9856765

00:32:03.620 --> 00:32:05.400 and it takes very accurate

NOTE Confidence: 0.9856765

00:32:05.460 --> 00:32:06.920 folding to make a heart.

NOTE Confidence: 0.9856765

00:32:07.060 --> 00:32:08.500 And also, once the heart

NOTE Confidence: 0.9856765

00:32:08.500 --> 00:32:09.940 starts at four weeks after

NOTE Confidence: 0.9856765

00:32:09.940 --> 00:32:10.440 fertilization,

NOTE Confidence: 0.9697913

00:32:11.125 --> 00:32:12.485 it continues to grow every

NOTE Confidence: 0.9697913

00:32:12.485 --> 00:32:14.085 day. It is beating at

NOTE Confidence: 0.9697913

00:32:14.085 --> 00:32:15.365 a hundred and fifty beats

NOTE Confidence: 0.9697913

00:32:15.365 --> 00:32:16.965 a minute, and it's getting

NOTE Confidence: 0.9697913

00:32:16.965 --> 00:32:18.645 larger. It's like building an

NOTE Confidence: 0.9697913

00:32:18.645 --> 00:32:20.325 airplane in midair while it's

NOTE Confidence: 0.9697913

00:32:20.325 --> 00:32:21.924 flying. That is a very

NOTE Confidence: 0.9697913

00:32:21.924 --> 00:32:24.085 sophisticated problem. So in my

NOTE Confidence: 0.9697913

00:32:24.085 --> 00:32:24.585 opinion,

NOTE Confidence: 0.9896764

00:32:25.230 --> 00:32:26.429 what I think is happening

NOTE Confidence: 0.9896764

00:32:26.429 --> 00:32:28.190 with these pregnancy losses is

NOTE Confidence: 0.9896764

00:32:28.190 --> 00:32:29.730 that they're related to abnormal

NOTE Confidence: 0.9896764

00:32:29.870 --> 00:32:30.610 heart folding.

NOTE Confidence: 0.99770516

00:32:31.070 --> 00:32:31.570 And

NOTE Confidence: 0.9965973

00:32:31.870 --> 00:32:32.850 I think that

NOTE Confidence: 0.9557572

00:32:33.150 --> 00:32:35.170 increased abnormalities of folding,

NOTE Confidence: 0.9901899

00:32:35.630 --> 00:32:36.990 as shown by this graph,

NOTE Confidence: 0.9901899

00:32:36.990 --> 00:32:38.690 are related to earlier losses,

NOTE Confidence: 0.99423456

00:32:39.085 --> 00:32:41.005 which is reflected in just

NOTE Confidence: 0.99423456

00:32:41.005 --> 00:32:42.605 the statistics of looking at

NOTE Confidence: 0.99423456

00:32:42.605 --> 00:32:43.665 pregnancy losses.

NOTE Confidence: 0.951829

00:32:44.285 --> 00:32:45.405 As anybody who is a

NOTE Confidence: 0.951829

00:32:45.405 --> 00:32:46.465 reproductive endocrinologist

NOTE Confidence: 0.95089525

00:32:46.845 --> 00:32:48.845 knows, extremely high number of

NOTE Confidence: 0.95089525

00:32:48.845 --> 00:32:50.145 empty sac losses

NOTE Confidence: 0.9579079

00:32:50.605 --> 00:32:51.645 probably in the first week

NOTE Confidence: 0.9579079

00:32:51.645 --> 00:32:52.605 or two, and I think

NOTE Confidence: 0.9579079

00:32:52.605 --> 00:32:53.665 those are simply

NOTE Confidence: 0.9923332

00:32:54.220 --> 00:32:55.820 an embryonic or simply an

NOTE Confidence: 0.9923332

00:32:55.820 --> 00:32:57.019 embryo that never had a

NOTE Confidence: 0.9923332

00:32:57.019 --> 00:32:58.460 heart that started. It didn't

NOTE Confidence: 0.9923332

00:32:58.460 --> 00:33:00.059 even start. If it starts

NOTE Confidence: 0.9923332

00:33:00.059 --> 00:33:01.179 at four weeks and then

NOTE Confidence: 0.9923332

00:33:01.179 --> 00:33:02.940 fails right away, then we

NOTE Confidence: 0.9923332

00:33:02.940 --> 00:33:04.380 have very early losses. And

NOTE Confidence: 0.9923332

00:33:04.380 --> 00:33:05.759 although we have a million

NOTE Confidence: 0.9923332

00:33:05.899 --> 00:33:06.399 miscarriages,

NOTE Confidence: 0.9681901

00:33:06.985 --> 00:33:08.505 I think we actually have

NOTE Confidence: 0.9681901

00:33:08.505 --> 00:33:10.345 even more losses before this

NOTE Confidence: 0.9681901

00:33:10.345 --> 00:33:11.225 period of time that we

NOTE Confidence: 0.9681901

00:33:11.225 --> 00:33:12.924 don't even know about. Right?

NOTE Confidence: 0.9681901

00:33:12.985 --> 00:33:14.764 I agree. Not even appreciated.

NOTE Confidence: 0.98289675

00:33:15.225 --> 00:33:16.264 And, again, what is the

NOTE Confidence: 0.98289675

00:33:16.264 --> 00:33:18.105 critical organ that's necessary? What

NOTE Confidence: 0.98289675

00:33:18.105 --> 00:33:19.304 do we look at when

NOTE Confidence: 0.98289675

00:33:19.304 --> 00:33:20.505 we define that you have

NOTE Confidence: 0.98289675

00:33:20.505 --> 00:33:21.164 a pregnancy?

NOTE Confidence: 0.98233545

00:33:21.480 --> 00:33:22.760 It's, of course, a heartbeat,

NOTE Confidence: 0.98233545

00:33:22.760 --> 00:33:23.880 right? That's what we're looking

NOTE Confidence: 0.98233545

00:33:23.880 --> 00:33:25.240 for. So I think that

NOTE Confidence: 0.98233545

00:33:25.240 --> 00:33:26.620 this is really where

NOTE Confidence: 0.9998379

00:33:27.080 --> 00:33:28.299 the answer is.

NOTE Confidence: 0.9897424

00:33:28.600 --> 00:33:29.799 The final piece of this

NOTE Confidence: 0.9897424

00:33:29.799 --> 00:33:30.840 puzzle that I'd like to

NOTE Confidence: 0.9897424

00:33:30.840 --> 00:33:32.200 share with you is an

NOTE Confidence: 0.9897424

00:33:32.200 --> 00:33:33.640 enigma that I've had. I've

NOTE Confidence: 0.9897424

00:33:33.640 --> 00:33:34.600 showed you that the number

NOTE Confidence: 0.9897424

00:33:34.600 --> 00:33:35.799 one cause of stillbirth is

NOTE Confidence: 0.9897424

00:33:35.799 --> 00:33:36.700 a small placenta.

NOTE Confidence: 0.9989484

00:33:37.215 --> 00:33:38.975 How could genetics relate to

NOTE Confidence: 0.9989484

00:33:38.975 --> 00:33:39.715 small placentas?

NOTE Confidence: 0.9991854

00:33:40.095 --> 00:33:40.595 Well,

NOTE Confidence: 0.9903897

00:33:41.215 --> 00:33:42.335 I think that it relates

NOTE Confidence: 0.9903897

00:33:42.335 --> 00:33:43.695 back to the heart, and

NOTE Confidence: 0.9903897

00:33:43.695 --> 00:33:44.735 that when you have an

NOTE Confidence: 0.9903897

00:33:44.735 --> 00:33:46.815 abnormal heart, the heart does

NOTE Confidence: 0.9903897

00:33:46.815 --> 00:33:48.414 not pump as well, has

NOTE Confidence: 0.9903897

00:33:48.414 --> 00:33:50.590 poor cardiac output, and does

NOTE Confidence: 0.9903897

00:33:50.590 --> 00:33:52.429 not literally blow up the

NOTE Confidence: 0.9903897

00:33:52.429 --> 00:33:52.929 placenta

NOTE Confidence: 0.99019367

00:33:53.309 --> 00:33:55.330 like a bicycle pump normally.

NOTE Confidence: 0.9699704

00:33:55.710 --> 00:33:56.830 So if you have a

NOTE Confidence: 0.9699704

00:33:56.830 --> 00:33:58.269 bicycle pump that is too

NOTE Confidence: 0.9699704

00:33:58.269 --> 00:34:00.130 small, and this is completely

NOTE Confidence: 0.9699704

00:34:00.269 --> 00:34:01.710 hypothetical, there is no evidence

NOTE Confidence: 0.9699704

00:34:01.710 --> 00:34:02.925 to support this at all.

NOTE Confidence: 0.9699704

00:34:03.245 --> 00:34:04.765 Although, Hugh, you'll remember the

NOTE Confidence: 0.9699704

00:34:04.765 --> 00:34:06.605 grant we submitted for our

NOTE Confidence: 0.9699704

00:34:06.605 --> 00:34:07.105 stillbirth

NOTE Confidence: 0.9765235

00:34:07.565 --> 00:34:10.445 included trophoblast inclusions, EPV, and

NOTE Confidence: 0.9765235

00:34:10.445 --> 00:34:12.385 looking at detailed heart structure.

NOTE Confidence: 0.9765235

00:34:12.605 --> 00:34:13.565 So I think that we're

NOTE Confidence: 0.9765235

00:34:13.565 --> 00:34:14.925 on the right track. Now

NOTE Confidence: 0.9765235

00:34:14.925 --> 00:34:16.045 is there evidence in the

NOTE Confidence: 0.9765235

00:34:16.045 --> 00:34:17.340 literature to support this? Well,

NOTE Confidence: 0.9765235

00:34:17.340 --> 00:34:19.020 there certainly is. Here's, for

NOTE Confidence: 0.9765235

00:34:19.020 --> 00:34:20.940 example, an article that said,

NOTE Confidence: 0.9765235

00:34:20.940 --> 00:34:22.720 among the few studies reported,

NOTE Confidence: 0.9923613

00:34:23.100 --> 00:34:24.540 several of these have noted

NOTE Confidence: 0.9923613

00:34:24.540 --> 00:34:26.460 smaller placentas in newborns with

NOTE Confidence: 0.9923613

00:34:26.460 --> 00:34:27.840 congenital heart disease.

NOTE Confidence: 0.95398426

00:34:28.300 --> 00:34:29.680 And Miriam Hamburger,

NOTE Confidence: 0.94363517

00:34:30.645 --> 00:34:31.925 who, Yong Hui, you had

NOTE Confidence: 0.94363517

00:34:31.925 --> 00:34:33.285 quoted one of her papers

NOTE Confidence: 0.94363517

00:34:33.285 --> 00:34:34.725 early in our study years

NOTE Confidence: 0.94363517

00:34:34.725 --> 00:34:36.245 ago. You might remember this

NOTE Confidence: 0.94363517

00:34:36.245 --> 00:34:37.305 paper that you,

NOTE Confidence: 0.9965637

00:34:37.765 --> 00:34:38.825 shared with everybody.

NOTE Confidence: 0.95805275

00:34:39.285 --> 00:34:40.565 What she showed, and I

NOTE Confidence: 0.95805275

00:34:40.565 --> 00:34:41.605 talked to her about this

NOTE Confidence: 0.95805275

00:34:41.605 --> 00:34:42.725 work, she said in the

NOTE Confidence: 0.95805275

00:34:42.725 --> 00:34:43.225 mouse,

NOTE Confidence: 0.9972693

00:34:43.530 --> 00:34:45.130 not all small placentas are

NOTE Confidence: 0.9972693

00:34:45.130 --> 00:34:46.910 associated with congenital heart disease,

NOTE Confidence: 0.9972693

00:34:47.130 --> 00:34:48.670 but all cases of congenital

NOTE Confidence: 0.9972693

00:34:48.730 --> 00:34:50.170 heart disease have a small

NOTE Confidence: 0.9972693

00:34:50.170 --> 00:34:51.610 placenta. So I think that's

NOTE Confidence: 0.9972693

00:34:51.610 --> 00:34:52.910 an interesting observation.

NOTE Confidence: 0.9737312

00:34:53.450 --> 00:34:54.910 So my question and

NOTE Confidence: 0.95807827

00:34:55.370 --> 00:34:56.270 final hypothesis

NOTE Confidence: 0.9681819

00:34:56.570 --> 00:34:57.690 to think about for the

NOTE Confidence: 0.9681819

00:34:57.690 --> 00:34:59.385 group here is are there

NOTE Confidence: 0.9681819

00:34:59.385 --> 00:35:01.305 common genes responsible for all

NOTE Confidence: 0.9681819

00:35:01.305 --> 00:35:04.205 these things? Trophoblast inclusions, abnormal

NOTE Confidence: 0.9681819

00:35:04.265 --> 00:35:05.705 folding, increased folding in the

NOTE Confidence: 0.9681819

00:35:05.705 --> 00:35:07.885 brain, dysmorphia features in embryos,

NOTE Confidence: 0.9707703

00:35:08.344 --> 00:35:10.825 pregnancy losses, abnormal hearts, are

NOTE Confidence: 0.9707703

00:35:10.825 --> 00:35:11.965 there common genes?

NOTE Confidence: 0.9642029

00:35:12.460 --> 00:35:14.140 And Miriam Hamburger, again, and

NOTE Confidence: 0.9642029

00:35:14.140 --> 00:35:14.940 this is the paper that

NOTE Confidence: 0.9642029

00:35:14.940 --> 00:35:16.060 you cited for us, young

NOTE Confidence: 0.9642029

00:35:16.060 --> 00:35:18.300 Weez, she said placental defects

NOTE Confidence: 0.9642029

00:35:18.300 --> 00:35:20.560 correlate strongly with abnormal brain,

NOTE Confidence: 0.9642029

00:35:20.620 --> 00:35:22.620 heart, and vascular development in

NOTE Confidence: 0.9642029

00:35:22.620 --> 00:35:24.800 these embryonic lethal mouse mutants.

NOTE Confidence: 0.9642029

00:35:24.860 --> 00:35:26.555 So that, I think, is

NOTE Confidence: 0.9642029

00:35:26.555 --> 00:35:28.075 where we are headed with

NOTE Confidence: 0.9642029

00:35:28.075 --> 00:35:28.575 gPRPL.

NOTE Confidence: 0.9626639

00:35:29.275 --> 00:35:30.395 I will just end with

NOTE Confidence: 0.9626639

00:35:30.395 --> 00:35:32.154 one final study that we're

NOTE Confidence: 0.9626639

00:35:32.154 --> 00:35:34.474 just hopefully finishing soon. Cindy

NOTE Confidence: 0.9626639

00:35:34.474 --> 00:35:35.694 Ortonau at

NOTE Confidence: 0.8511908

00:35:35.994 --> 00:35:37.994 University of Washington Washington University

NOTE Confidence: 0.8511908

00:35:37.994 --> 00:35:39.135 in Saint Louis, sorry.

NOTE Confidence: 0.9819733

00:35:39.660 --> 00:35:41.359 She looks at the brain

NOTE Confidence: 0.9819733

00:35:41.420 --> 00:35:42.559 heart connection.

NOTE Confidence: 0.9960879

00:35:43.020 --> 00:35:44.300 I asked her to look

NOTE Confidence: 0.9960879

00:35:44.300 --> 00:35:45.180 at if I could look

NOTE Confidence: 0.9960879

00:35:45.180 --> 00:35:46.000 at the placentas

NOTE Confidence: 0.99961376

00:35:46.460 --> 00:35:47.440 from her cases

NOTE Confidence: 0.97837013

00:35:48.380 --> 00:35:50.140 of congenital heart disease and

NOTE Confidence: 0.97837013

00:35:50.140 --> 00:35:52.075 abnormal brain development, and we

NOTE Confidence: 0.97837013

00:35:52.075 --> 00:35:53.594 have shown that there's a

NOTE Confidence: 0.97837013

00:35:53.594 --> 00:35:56.015 significant increase of tropholast inclusions

NOTE Confidence: 0.97837013

00:35:56.155 --> 00:35:57.675 in the placenta of children

NOTE Confidence: 0.97837013

00:35:57.675 --> 00:35:59.515 with congenital heart disease. So

NOTE Confidence: 0.97837013

00:35:59.515 --> 00:36:01.295 I think the unifying hypothesis

NOTE Confidence: 0.999219

00:36:01.675 --> 00:36:02.715 might be that there are

NOTE Confidence: 0.999219

00:36:02.715 --> 00:36:04.815 shared genes related to congenital

NOTE Confidence: 0.999219

00:36:04.875 --> 00:36:05.535 heart disease,

NOTE Confidence: 0.9978316

00:36:06.180 --> 00:36:06.920 folding morphogenesis,

NOTE Confidence: 0.9998888

00:36:07.460 --> 00:36:08.440 branching morphogenesis,

NOTE Confidence: 0.99890584

00:36:08.819 --> 00:36:10.599 pregnancy loss, intelligence,

NOTE Confidence: 0.9945064

00:36:10.900 --> 00:36:11.400 developmental

NOTE Confidence: 0.90120655

00:36:11.700 --> 00:36:13.160 disabilities such as autism.

NOTE Confidence: 0.98977304

00:36:13.700 --> 00:36:15.619 And what I'm hoping is

NOTE Confidence: 0.98977304

00:36:15.619 --> 00:36:17.140 that in our studies, we

NOTE Confidence: 0.98977304

00:36:17.140 --> 00:36:18.660 can identify some of these

NOTE Confidence: 0.98977304

00:36:18.660 --> 00:36:19.560 common genes.

NOTE Confidence: 0.9703748

00:36:19.994 --> 00:36:21.275 Now this work is done

NOTE Confidence: 0.9703748

00:36:21.275 --> 00:36:22.875 with many, many, many people

NOTE Confidence: 0.9703748

00:36:22.875 --> 00:36:24.234 involved, including, of course, the

NOTE Confidence: 0.9703748

00:36:24.234 --> 00:36:24.734 GPR

NOTE Confidence: 0.97414255

00:36:25.035 --> 00:36:26.974 group right here, the trophoblast

NOTE Confidence: 0.97414255

00:36:27.114 --> 00:36:28.795 inclusion group, my pregnancy loss

NOTE Confidence: 0.97414255

00:36:28.795 --> 00:36:30.974 group, and Cindy Ortonau's group

NOTE Confidence: 0.97414255

00:36:31.035 --> 00:36:31.535 at

NOTE Confidence: 0.9682677

00:36:31.930 --> 00:36:33.370 University of Washington. I'd like

NOTE Confidence: 0.9682677

00:36:33.370 --> 00:36:34.810 to acknowledge them. And for

NOTE Confidence: 0.9682677

00:36:34.810 --> 00:36:36.330 anybody who is interested in

NOTE Confidence: 0.9682677

00:36:36.330 --> 00:36:37.530 any details of what I've

NOTE Confidence: 0.9682677

00:36:37.530 --> 00:36:38.969 talked about, please feel free

NOTE Confidence: 0.9682677

00:36:38.969 --> 00:36:40.010 to email me or go

NOTE Confidence: 0.9682677

00:36:40.010 --> 00:36:41.530 to my lab site here

NOTE Confidence: 0.9682677

00:36:41.530 --> 00:36:42.730 at yale, klein and labs

NOTE Confidence: 0.9682677

00:36:42.730 --> 00:36:43.850 dot yale dot edu. And,

NOTE Confidence: 0.9682677

00:36:43.850 --> 00:36:45.075 again, I put this out

NOTE Confidence: 0.9682677

00:36:45.075 --> 00:36:46.675 to anybody who has any

NOTE Confidence: 0.9682677

00:36:46.675 --> 00:36:48.435 patients with pregnancy loss. I

NOTE Confidence: 0.9682677

00:36:48.435 --> 00:36:50.114 would welcome very much looking

NOTE Confidence: 0.9682677

00:36:50.114 --> 00:36:51.395 at those cases and helping

NOTE Confidence: 0.9682677

00:36:51.395 --> 00:36:52.515 you with them. Thank you

NOTE Confidence: 0.9682677

00:36:52.515 --> 00:36:53.555 very much for letting me

NOTE Confidence: 0.9682677

00:36:53.555 --> 00:36:54.594 share my work with you

NOTE Confidence: 0.9682677

00:36:54.594 --> 00:36:55.094 today.

NOTE Confidence: 0.85688275

00:36:59.830 --> 00:37:01.450 Thank you, Hugh. Hey, Warwick.

NOTE Confidence: 0.982612

00:37:01.830 --> 00:37:02.330 Amazing.

NOTE Confidence: 0.81780165

00:37:03.830 --> 00:37:04.790 Well How do you bring

NOTE Confidence: 0.81780165

00:37:04.790 --> 00:37:05.690 it all together?

NOTE Confidence: 0.9407964

00:37:06.710 --> 00:37:07.750 I like a lot of

NOTE Confidence: 0.9407964

00:37:07.750 --> 00:37:08.250 quote,

NOTE Confidence: 0.9364761

00:37:08.550 --> 00:37:09.050 Harvey.

NOTE Confidence: 0.759048

00:37:09.750 --> 00:37:10.489 That's a

NOTE Confidence: 0.82481176

00:37:11.094 --> 00:37:12.695 history. I I have a

NOTE Confidence: 0.82481176

00:37:12.935 --> 00:37:14.935 how you're looking for, sort

NOTE Confidence: 0.82481176

00:37:14.935 --> 00:37:15.735 of what would be the

NOTE Confidence: 0.82481176

00:37:15.735 --> 00:37:17.594 next step to for this

NOTE Confidence: 0.5802279

00:37:18.215 --> 00:37:18.715 study.

NOTE Confidence: 0.8206397

00:37:19.335 --> 00:37:20.535 How many of for case

NOTE Confidence: 0.8206397

00:37:20.535 --> 00:37:21.495 you have fresh,

NOTE Confidence: 0.79725856

00:37:23.175 --> 00:37:24.875 percent store in

NOTE Confidence: 0.8591441

00:37:26.300 --> 00:37:27.900 minus eighty or or or

NOTE Confidence: 0.8591441

00:37:27.900 --> 00:37:29.420 liquid nitrogen, would you able

NOTE Confidence: 0.8591441

00:37:29.420 --> 00:37:31.200 to do the RNA expression

NOTE Confidence: 0.8591441

00:37:31.340 --> 00:37:31.840 study?

NOTE Confidence: 0.9975276

00:37:33.180 --> 00:37:34.000 Yeah. Unfortunately,

NOTE Confidence: 0.9926104

00:37:35.260 --> 00:37:37.359 my relationship with my patients

NOTE Confidence: 0.9926104

00:37:37.580 --> 00:37:39.420 is and, actually, COVID is

NOTE Confidence: 0.9926104

00:37:39.420 --> 00:37:41.520 partly it's interesting. Before COVID,

NOTE Confidence: 0.9926104

00:37:41.785 --> 00:37:43.225 I saw very few pregnancy

NOTE Confidence: 0.9926104

00:37:43.225 --> 00:37:44.505 loss patients because they had

NOTE Confidence: 0.9926104

00:37:44.505 --> 00:37:46.185 to physically be in Connecticut

NOTE Confidence: 0.9926104

00:37:46.185 --> 00:37:47.145 or come to Yale to

NOTE Confidence: 0.9926104

00:37:47.145 --> 00:37:47.885 see me.

NOTE Confidence: 0.9876481

00:37:48.185 --> 00:37:50.045 COVID opened up the opportunity

NOTE Confidence: 0.9876481

00:37:50.105 --> 00:37:51.065 for me to start seeing

NOTE Confidence: 0.9876481

00:37:51.065 --> 00:37:52.344 patients all over the world,

NOTE Confidence: 0.9876481

00:37:52.344 --> 00:37:52.844 literally.

NOTE Confidence: 0.988564

00:37:53.305 --> 00:37:55.070 So I now have a

NOTE Confidence: 0.988564

00:37:55.070 --> 00:37:56.910 reputation that really draws from

NOTE Confidence: 0.988564

00:37:56.910 --> 00:37:58.670 all over, and the negative

NOTE Confidence: 0.988564

00:37:58.670 --> 00:38:00.130 is that my patients

NOTE Confidence: 0.9988863

00:38:00.510 --> 00:38:02.110 are seeking me out after

NOTE Confidence: 0.9988863

00:38:02.110 --> 00:38:03.650 they've tried to get answers

NOTE Confidence: 0.9988863

00:38:03.710 --> 00:38:04.210 locally.

NOTE Confidence: 0.9767383

00:38:04.510 --> 00:38:05.469 And when they can't get

NOTE Confidence: 0.9767383

00:38:05.469 --> 00:38:06.989 an answer locally, they find

NOTE Confidence: 0.9767383

00:38:06.989 --> 00:38:08.190 me, like the first case

NOTE Confidence: 0.9767383

00:38:08.190 --> 00:38:09.725 I showed you. And those

NOTE Confidence: 0.9767383

00:38:09.725 --> 00:38:11.725 cases, the placentas are fixed

NOTE Confidence: 0.9767383

00:38:11.725 --> 00:38:12.385 in formalin.

NOTE Confidence: 0.959431

00:38:12.765 --> 00:38:13.965 So that is why in

NOTE Confidence: 0.959431

00:38:13.965 --> 00:38:15.645 the very beginning of this,

NOTE Confidence: 0.99400866

00:38:16.125 --> 00:38:16.625 study,

NOTE Confidence: 0.9996801

00:38:16.925 --> 00:38:18.145 I was so grateful

NOTE Confidence: 0.92969906

00:38:18.525 --> 00:38:20.285 that the Yale Genomic Center

NOTE Confidence: 0.92969906

00:38:20.285 --> 00:38:21.565 and Monkel, I have to

NOTE Confidence: 0.92969906

00:38:21.565 --> 00:38:22.605 thank him and his whole

NOTE Confidence: 0.92969906

00:38:22.605 --> 00:38:23.505 team and everybody,

NOTE Confidence: 0.98191667

00:38:24.410 --> 00:38:25.690 you know, who was involved

NOTE Confidence: 0.98191667

00:38:25.690 --> 00:38:27.550 with this, to figure out

NOTE Confidence: 0.98191667

00:38:27.690 --> 00:38:29.230 how to actually do decent,

NOTE Confidence: 0.98191667

00:38:29.290 --> 00:38:31.390 not fantastic, but decent genomic

NOTE Confidence: 0.98191667

00:38:31.450 --> 00:38:33.710 analysis of paraffin embedded tissue

NOTE Confidence: 0.98191667

00:38:33.930 --> 00:38:35.610 because it is very difficult

NOTE Confidence: 0.98191667

00:38:35.610 --> 00:38:36.810 to get that fresh loss

NOTE Confidence: 0.98191667

00:38:36.810 --> 00:38:37.930 on these patients as we

NOTE Confidence: 0.98191667

00:38:37.930 --> 00:38:39.614 know. So that's, I think,

NOTE Confidence: 0.98191667

00:38:39.614 --> 00:38:40.895 the limiting factor. If there's

NOTE Confidence: 0.98191667

00:38:40.895 --> 00:38:41.855 a way for anybody to

NOTE Confidence: 0.98191667

00:38:41.855 --> 00:38:42.815 figure out how to solve

NOTE Confidence: 0.98191667

00:38:42.815 --> 00:38:43.315 that,

NOTE Confidence: 0.9768798

00:38:43.614 --> 00:38:44.655 yes. We should try to

NOTE Confidence: 0.9768798

00:38:44.655 --> 00:38:46.015 do it. But I I

NOTE Confidence: 0.9768798

00:38:46.015 --> 00:38:47.135 go where the light bulb

NOTE Confidence: 0.9768798

00:38:47.135 --> 00:38:48.094 is shining at night, you

NOTE Confidence: 0.9768798

00:38:48.094 --> 00:38:49.055 know, the old adage of

NOTE Confidence: 0.9768798

00:38:49.055 --> 00:38:50.015 the old man losing the

NOTE Confidence: 0.9768798

00:38:50.015 --> 00:38:51.215 keys. You know? You look

NOTE Confidence: 0.9768798

00:38:51.215 --> 00:38:52.255 where the light bulb is

NOTE Confidence: 0.9768798

00:38:52.255 --> 00:38:53.695 shining. That's always been my

NOTE Confidence: 0.9768798

00:38:53.695 --> 00:38:54.195 philosophy.

NOTE Confidence: 0.95881134

00:38:55.589 --> 00:38:56.950 Harvey, to date, I mean,

NOTE Confidence: 0.95881134

00:38:56.950 --> 00:38:58.309 of the ones of your

NOTE Confidence: 0.95881134

00:38:58.309 --> 00:38:58.809 specimens

NOTE Confidence: 0.99945694

00:38:59.109 --> 00:39:00.010 that have been

NOTE Confidence: 0.972331

00:39:00.469 --> 00:39:02.390 sequenced, have the ones that

NOTE Confidence: 0.972331

00:39:02.390 --> 00:39:04.390 have shown some evidence of

NOTE Confidence: 0.972331

00:39:04.390 --> 00:39:06.390 mutation been particularly extreme in

NOTE Confidence: 0.972331

00:39:06.390 --> 00:39:07.910 the number of inclusions they've

NOTE Confidence: 0.972331

00:39:07.910 --> 00:39:08.710 had, or are there any

NOTE Confidence: 0.972331

00:39:08.710 --> 00:39:09.690 correlation there?

NOTE Confidence: 0.9811559

00:39:10.355 --> 00:39:11.954 Well, it's interesting you asked

NOTE Confidence: 0.9811559

00:39:11.954 --> 00:39:13.714 that. Every patient that I

NOTE Confidence: 0.9811559

00:39:13.714 --> 00:39:15.015 have submitted to GPRPL

NOTE Confidence: 0.9414173

00:39:15.635 --> 00:39:17.234 has truffle blast inclusions. That

NOTE Confidence: 0.9414173

00:39:17.234 --> 00:39:18.434 is the that is the

NOTE Confidence: 0.9414173

00:39:18.434 --> 00:39:18.915 criteria.

NOTE Confidence: 0.9201604

00:39:19.395 --> 00:39:20.295 Huge variability.

NOTE Confidence: 0.9859339

00:39:20.915 --> 00:39:21.895 There is a variability.

NOTE Confidence: 0.9651416

00:39:22.739 --> 00:39:23.780 Conclusions. I thought what you

NOTE Confidence: 0.9651416

00:39:23.780 --> 00:39:24.820 were gonna ask was something

NOTE Confidence: 0.9651416

00:39:24.820 --> 00:39:26.440 slightly different, so I,

NOTE Confidence: 0.8776765

00:39:27.219 --> 00:39:28.500 just allow me this,

NOTE Confidence: 0.971168

00:39:28.820 --> 00:39:30.440 to change your question slightly.

NOTE Confidence: 0.971168

00:39:30.660 --> 00:39:32.580 Have we even found any

NOTE Confidence: 0.971168

00:39:32.580 --> 00:39:34.420 genetic genes in my two

NOTE Confidence: 0.971168

00:39:34.420 --> 00:39:35.875 hundred or so patients? And

NOTE Confidence: 0.971168

00:39:35.875 --> 00:39:37.475 I'm gonna let Monkel speak

NOTE Confidence: 0.971168

00:39:37.475 --> 00:39:38.995 to that. He and Andrew

NOTE Confidence: 0.971168

00:39:38.995 --> 00:39:40.275 and I meet, you know,

NOTE Confidence: 0.971168

00:39:40.275 --> 00:39:41.395 every few weeks to go

NOTE Confidence: 0.971168

00:39:41.395 --> 00:39:42.375 over my patients.

NOTE Confidence: 0.99676776

00:39:42.915 --> 00:39:43.415 And,

NOTE Confidence: 0.9906223

00:39:44.435 --> 00:39:45.315 you know, there have been

NOTE Confidence: 0.9906223

00:39:45.315 --> 00:39:46.355 some that we have found

NOTE Confidence: 0.9906223

00:39:46.355 --> 00:39:48.835 some answers. I'm surprised still

NOTE Confidence: 0.9906223

00:39:48.835 --> 00:39:49.955 at how few we have

NOTE Confidence: 0.9906223

00:39:49.955 --> 00:39:51.890 found answers to, but I'm

NOTE Confidence: 0.9906223

00:39:51.890 --> 00:39:52.390 hoping

NOTE Confidence: 0.9014059

00:39:52.690 --> 00:39:53.969 that we will find them

NOTE Confidence: 0.9014059

00:39:53.969 --> 00:39:55.810 and continued analysis will work.

NOTE Confidence: 0.9014059

00:39:55.810 --> 00:39:57.010 Michael, do you wanna jump

NOTE Confidence: 0.9014059

00:39:57.010 --> 00:39:57.410 in and give me an

NOTE Confidence: 0.9014059

00:39:57.410 --> 00:39:57.910 overview

NOTE Confidence: 0.9707157

00:39:58.690 --> 00:40:00.050 of that? So so one

NOTE Confidence: 0.9707157

00:40:00.050 --> 00:40:01.170 of the analysis on the

NOTE Confidence: 0.9707157

00:40:01.170 --> 00:40:02.930 to do list, okay, the

NOTE Confidence: 0.9707157

00:40:03.090 --> 00:40:04.130 a low hanging fruit is

NOTE Confidence: 0.9707157

00:40:04.130 --> 00:40:05.510 to ask the question of

NOTE Confidence: 0.9707157

00:40:05.614 --> 00:40:06.734 a lot of genes are

NOTE Confidence: 0.9707157

00:40:06.734 --> 00:40:08.494 expressed in the placenta and

NOTE Confidence: 0.9707157

00:40:08.494 --> 00:40:09.635 the, you know, the placenta

NOTE Confidence: 0.9707157

00:40:09.694 --> 00:40:11.535 material. So, you know, the

NOTE Confidence: 0.9707157

00:40:11.535 --> 00:40:12.815 the first low hanging fruit

NOTE Confidence: 0.9707157

00:40:12.815 --> 00:40:14.815 is a direct genetic influence.

NOTE Confidence: 0.9707157

00:40:14.815 --> 00:40:16.755 So genes that cause disease

NOTE Confidence: 0.9707157

00:40:16.895 --> 00:40:19.055 and are also important in

NOTE Confidence: 0.9707157

00:40:19.055 --> 00:40:20.434 the expression in,

NOTE Confidence: 0.92839724

00:40:20.920 --> 00:40:22.600 placenta. Like, Hugh, you remember

NOTE Confidence: 0.92839724

00:40:22.600 --> 00:40:24.120 when I, when we presented

NOTE Confidence: 0.92839724

00:40:24.120 --> 00:40:25.239 the NIH, one of them

NOTE Confidence: 0.92839724

00:40:25.239 --> 00:40:26.680 were a gene that was

NOTE Confidence: 0.92839724

00:40:26.680 --> 00:40:28.460 very important for vascular

NOTE Confidence: 0.7567992

00:40:29.160 --> 00:40:29.660 vascularization

NOTE Confidence: 0.97631073

00:40:30.680 --> 00:40:32.300 of the of the placenta.

NOTE Confidence: 0.97631073

00:40:32.440 --> 00:40:34.040 So it's not only important

NOTE Confidence: 0.97631073

00:40:34.040 --> 00:40:35.239 placenta, but it's, you know,

NOTE Confidence: 0.97631073

00:40:35.239 --> 00:40:36.975 important in general too. But,

NOTE Confidence: 0.97631073

00:40:36.975 --> 00:40:38.815 you know, but it does

NOTE Confidence: 0.97631073

00:40:38.815 --> 00:40:40.415 cause a big problem early

NOTE Confidence: 0.97631073

00:40:40.415 --> 00:40:42.255 development. So so I think

NOTE Confidence: 0.97631073

00:40:42.255 --> 00:40:43.695 the next low hanging fruit

NOTE Confidence: 0.97631073

00:40:43.695 --> 00:40:45.395 is asking the questions, okay,

NOTE Confidence: 0.9412999

00:40:45.855 --> 00:40:47.395 we know these genes cause,

NOTE Confidence: 0.9412999

00:40:47.535 --> 00:40:49.695 you know, severe diseases or

NOTE Confidence: 0.9412999

00:40:49.695 --> 00:40:51.135 these are strong candidates, one

NOTE Confidence: 0.9412999

00:40:51.135 --> 00:40:52.350 or the other, one of

NOTE Confidence: 0.9412999

00:40:52.350 --> 00:40:53.630 the what are their expression

NOTE Confidence: 0.9412999

00:40:53.630 --> 00:40:54.750 levels like? And we can

NOTE Confidence: 0.9412999

00:40:54.750 --> 00:40:55.650 go one further,

NOTE Confidence: 0.8898655

00:40:55.950 --> 00:40:56.850 Harvey, because

NOTE Confidence: 0.98256797

00:40:57.230 --> 00:40:58.910 in preparing the stillbirth grant

NOTE Confidence: 0.98256797

00:40:58.910 --> 00:41:00.050 last year yeah.

NOTE Confidence: 0.94621825

00:41:00.750 --> 00:41:02.350 Still still the trauma of

NOTE Confidence: 0.94621825

00:41:02.350 --> 00:41:02.850 chasing

NOTE Confidence: 0.8775853

00:41:03.630 --> 00:41:04.610 chasing signatures,

NOTE Confidence: 0.9172095

00:41:05.825 --> 00:41:07.025 you know, one hour before

NOTE Confidence: 0.9172095

00:41:07.025 --> 00:41:08.945 submissions. It's still burned in

NOTE Confidence: 0.9172095

00:41:08.945 --> 00:41:10.545 my head. But one one

NOTE Confidence: 0.9172095

00:41:10.545 --> 00:41:11.585 of the things that,

NOTE Confidence: 0.9594168

00:41:11.985 --> 00:41:13.665 that the field has done,

NOTE Confidence: 0.9594168

00:41:13.665 --> 00:41:15.185 you know, and this is

NOTE Confidence: 0.9594168

00:41:15.185 --> 00:41:16.545 my gonna be my question

NOTE Confidence: 0.9594168

00:41:16.545 --> 00:41:17.745 to you, Harvey, because it's

NOTE Confidence: 0.9594168

00:41:17.745 --> 00:41:19.265 related to what Yonghui said

NOTE Confidence: 0.9594168

00:41:19.265 --> 00:41:21.089 is they've done some really

NOTE Confidence: 0.9594168

00:41:21.089 --> 00:41:23.250 great single nuclei work. So

NOTE Confidence: 0.9594168

00:41:23.250 --> 00:41:25.349 frozen placenta. And because

NOTE Confidence: 0.97085273

00:41:25.730 --> 00:41:27.089 of the property you're saying,

NOTE Confidence: 0.97085273

00:41:27.089 --> 00:41:28.369 it's very similar to,

NOTE Confidence: 0.9838955

00:41:28.849 --> 00:41:30.450 to muscle fibers. You have

NOTE Confidence: 0.9838955

00:41:30.450 --> 00:41:32.450 multiple nuclei sharing the same

NOTE Confidence: 0.9838955

00:41:32.450 --> 00:41:32.950 cytoplasm.

NOTE Confidence: 0.9571223

00:41:34.615 --> 00:41:36.375 So single nuclei work really

NOTE Confidence: 0.9571223

00:41:36.375 --> 00:41:37.255 well in that, and they've

NOTE Confidence: 0.9571223

00:41:37.255 --> 00:41:38.695 done some single nuclei that

NOTE Confidence: 0.9571223

00:41:38.695 --> 00:41:39.735 was published about a year

NOTE Confidence: 0.9571223

00:41:39.735 --> 00:41:40.375 and a half ago in

NOTE Confidence: 0.9571223

00:41:40.375 --> 00:41:41.275 Nature Genetics.

NOTE Confidence: 0.97102964

00:41:41.735 --> 00:41:43.415 So one of the cool

NOTE Confidence: 0.97102964

00:41:43.415 --> 00:41:44.775 things we could do, you

NOTE Confidence: 0.97102964

00:41:44.775 --> 00:41:45.615 know what I mean,

NOTE Confidence: 0.95087516

00:41:46.055 --> 00:41:46.555 if,

NOTE Confidence: 0.96058637

00:41:47.095 --> 00:41:47.595 if,

NOTE Confidence: 0.8837119

00:41:48.090 --> 00:41:49.610 you know, you can correct

NOTE Confidence: 0.8837119

00:41:49.610 --> 00:41:50.510 me if I'm wrong.

NOTE Confidence: 0.9574272

00:41:51.210 --> 00:41:52.489 You know, in preparing it,

NOTE Confidence: 0.9574272

00:41:52.609 --> 00:41:54.030 I think Lina and I,

NOTE Confidence: 0.9975288

00:41:54.970 --> 00:41:55.550 know that

NOTE Confidence: 0.89172435

00:41:55.930 --> 00:41:57.870 Yale has a placenta

NOTE Confidence: 0.9793541

00:41:58.170 --> 00:41:59.850 biobank or something like that.

NOTE Confidence: 0.9793541

00:41:59.850 --> 00:42:00.350 And

NOTE Confidence: 0.97649914

00:42:00.795 --> 00:42:02.635 and if there are some

NOTE Confidence: 0.97649914

00:42:02.635 --> 00:42:03.434 that you know what I

NOTE Confidence: 0.97649914

00:42:03.434 --> 00:42:05.295 mean? That are you know

NOTE Confidence: 0.9151082

00:42:05.594 --> 00:42:06.555 you know how you had

NOTE Confidence: 0.9151082

00:42:06.555 --> 00:42:07.994 that model, Harvey, of, you

NOTE Confidence: 0.9151082

00:42:07.994 --> 00:42:09.755 know, the three possibilities. Normal

NOTE Confidence: 0.9151082

00:42:09.755 --> 00:42:10.555 is in the middle, and

NOTE Confidence: 0.9151082

00:42:10.555 --> 00:42:11.675 this can happen. This can

NOTE Confidence: 0.9151082

00:42:11.675 --> 00:42:12.974 happen. If we can get

NOTE Confidence: 0.9151082

00:42:13.114 --> 00:42:14.234 examples of that, and we

NOTE Confidence: 0.9151082

00:42:14.234 --> 00:42:15.675 can ask the question of,

NOTE Confidence: 0.9151082

00:42:15.675 --> 00:42:16.255 is there

NOTE Confidence: 0.92265445

00:42:16.839 --> 00:42:18.760 gen a genetic signature? If

NOTE Confidence: 0.92265445

00:42:18.760 --> 00:42:20.440 we did single nuclei sequencing

NOTE Confidence: 0.92265445

00:42:20.520 --> 00:42:21.400 I don't have the money.

NOTE Confidence: 0.92265445

00:42:21.400 --> 00:42:22.599 I'm hoping someone this call

NOTE Confidence: 0.92265445

00:42:22.599 --> 00:42:23.480 does, they can pay for

NOTE Confidence: 0.92265445

00:42:23.480 --> 00:42:23.980 it.

NOTE Confidence: 0.98215765

00:42:24.440 --> 00:42:25.800 If we did single nuclei

NOTE Confidence: 0.98215765

00:42:25.800 --> 00:42:27.079 sequencing on,

NOTE Confidence: 0.9824522

00:42:27.400 --> 00:42:27.900 placentas

NOTE Confidence: 0.9960431

00:42:28.200 --> 00:42:29.020 from this,

NOTE Confidence: 0.9044778

00:42:29.480 --> 00:42:30.885 then we can use, for

NOTE Confidence: 0.9044778

00:42:30.885 --> 00:42:32.825 example, the publication Nature's Genetics.

NOTE Confidence: 0.97535133

00:42:33.205 --> 00:42:34.485 This is how this is

NOTE Confidence: 0.97535133

00:42:34.485 --> 00:42:36.505 how healthy placenta should behave.

NOTE Confidence: 0.97535133

00:42:36.565 --> 00:42:37.765 We can create our own

NOTE Confidence: 0.97535133

00:42:37.765 --> 00:42:39.445 controls and ask that question

NOTE Confidence: 0.97535133

00:42:39.445 --> 00:42:40.245 of you know what I

NOTE Confidence: 0.97535133

00:42:40.245 --> 00:42:42.025 mean? But the genetic signature

NOTE Confidence: 0.97535133

00:42:42.165 --> 00:42:43.625 could be in response

NOTE Confidence: 0.933823

00:42:44.210 --> 00:42:45.089 or it could be the

NOTE Confidence: 0.933823

00:42:45.089 --> 00:42:46.130 driver, but it will still

NOTE Confidence: 0.933823

00:42:46.130 --> 00:42:47.329 be a genetic signature. And

NOTE Confidence: 0.933823

00:42:47.329 --> 00:42:48.690 it will give us more

NOTE Confidence: 0.933823

00:42:48.690 --> 00:42:50.150 of a feel for that

NOTE Confidence: 0.94175804

00:42:50.849 --> 00:42:52.369 mechanism behind what you were

NOTE Confidence: 0.94175804

00:42:52.369 --> 00:42:53.089 saying. You know what I

NOTE Confidence: 0.94175804

00:42:53.089 --> 00:42:54.049 mean? Or just say, you

NOTE Confidence: 0.94175804

00:42:54.049 --> 00:42:55.430 know, what is the genetics

NOTE Confidence: 0.94175804

00:42:55.489 --> 00:42:56.855 behind that mechanism. For some

NOTE Confidence: 0.94175804

00:42:56.855 --> 00:42:58.214 of that mechanism could be

NOTE Confidence: 0.94175804

00:42:58.214 --> 00:42:59.414 purely as you, I think,

NOTE Confidence: 0.94175804

00:42:59.414 --> 00:43:01.015 hinted Harvey. It could be

NOTE Confidence: 0.94175804

00:43:01.015 --> 00:43:02.535 purely physical, but it could

NOTE Confidence: 0.94175804

00:43:02.535 --> 00:43:04.295 be a physical thing, and

NOTE Confidence: 0.94175804

00:43:04.295 --> 00:43:06.075 then there's a genetic response

NOTE Confidence: 0.94175804

00:43:06.135 --> 00:43:07.674 to it or vice versa,

NOTE Confidence: 0.96106476

00:43:08.214 --> 00:43:09.174 you know, a chicken egg.

NOTE Confidence: 0.96106476

00:43:09.174 --> 00:43:10.135 But it'd be a cool

NOTE Confidence: 0.96106476

00:43:10.135 --> 00:43:11.255 thing we could do. You

NOTE Confidence: 0.96106476

00:43:11.255 --> 00:43:12.219 know what I mean? Since,

NOTE Confidence: 0.96106476

00:43:12.219 --> 00:43:13.040 you know,

NOTE Confidence: 0.972638

00:43:13.580 --> 00:43:15.500 it's only become available, this

NOTE Confidence: 0.972638

00:43:15.500 --> 00:43:16.860 technology, to do something like

NOTE Confidence: 0.972638

00:43:16.860 --> 00:43:18.140 that. I'd like to try

NOTE Confidence: 0.972638

00:43:18.140 --> 00:43:19.600 on that before the FFPE.

NOTE Confidence: 0.9823889

00:43:20.380 --> 00:43:21.980 But but me saying this,

NOTE Confidence: 0.9823889

00:43:21.980 --> 00:43:23.340 I I we would need

NOTE Confidence: 0.9823889

00:43:23.340 --> 00:43:24.540 money to do this, but

NOTE Confidence: 0.9823889

00:43:24.540 --> 00:43:25.820 it'd be an awesome question

NOTE Confidence: 0.9823889

00:43:25.820 --> 00:43:26.895 to ask, you know, based

NOTE Confidence: 0.9823889

00:43:26.895 --> 00:43:28.515 on your presentation, Harvey.

NOTE Confidence: 0.9534605

00:43:28.895 --> 00:43:30.355 Thank you. That sounds awesome.

NOTE Confidence: 0.9534605

00:43:30.575 --> 00:43:31.614 But my question was really

NOTE Confidence: 0.9534605

00:43:31.614 --> 00:43:33.055 more the ones you've that

NOTE Confidence: 0.9534605

00:43:33.055 --> 00:43:34.435 we have found some mutations

NOTE Confidence: 0.9534605

00:43:34.495 --> 00:43:35.535 in the samples you do

NOTE Confidence: 0.9534605

00:43:35.535 --> 00:43:36.735 have, were they, you know,

NOTE Confidence: 0.9534605

00:43:36.735 --> 00:43:38.015 were they just loaded with

NOTE Confidence: 0.9534605

00:43:38.015 --> 00:43:39.215 inclusions? Were they the real

NOTE Confidence: 0.9534605

00:43:39.215 --> 00:43:39.715 extremes?

NOTE Confidence: 0.97270966

00:43:40.710 --> 00:43:42.070 Right. So I have to

NOTE Confidence: 0.97270966

00:43:42.070 --> 00:43:43.350 admit I haven't done that

NOTE Confidence: 0.97270966

00:43:43.350 --> 00:43:43.850 because

NOTE Confidence: 0.96554065

00:43:44.550 --> 00:43:45.210 and, again,

NOTE Confidence: 0.9500201

00:43:45.590 --> 00:43:46.630 Andrew, I don't see him

NOTE Confidence: 0.9500201

00:43:46.630 --> 00:43:47.910 on the call, and Monkel

NOTE Confidence: 0.9500201

00:43:47.910 --> 00:43:49.350 and Ira. I I would

NOTE Confidence: 0.9500201

00:43:49.350 --> 00:43:50.710 love to sit down and

NOTE Confidence: 0.9500201

00:43:50.710 --> 00:43:52.570 actually, at some point, collect

NOTE Confidence: 0.98072314

00:43:53.205 --> 00:43:54.565 all of the cases that

NOTE Confidence: 0.98072314

00:43:54.565 --> 00:43:56.585 I have, you know, pathology

NOTE Confidence: 0.98072314

00:43:56.725 --> 00:43:57.945 on and I've looked at.

NOTE Confidence: 0.9687901

00:43:58.245 --> 00:43:59.844 What are the genetic results

NOTE Confidence: 0.9687901

00:43:59.844 --> 00:44:01.285 that we've gotten? There aren't

NOTE Confidence: 0.9687901

00:44:01.285 --> 00:44:02.245 that many. That's why I

NOTE Confidence: 0.9687901

00:44:02.245 --> 00:44:03.285 was hoping Oh, it's not

NOTE Confidence: 0.9687901

00:44:03.285 --> 00:44:04.245 many. But if what if

NOTE Confidence: 0.9687901

00:44:04.245 --> 00:44:05.364 what if those you know,

NOTE Confidence: 0.9687901

00:44:05.364 --> 00:44:06.645 one we found was the

NOTE Confidence: 0.9687901

00:44:06.645 --> 00:44:07.839 one that had, you know,

NOTE Confidence: 0.9687901

00:44:07.839 --> 00:44:09.359 hundred times more occlusions. We

NOTE Confidence: 0.9687901

00:44:09.359 --> 00:44:10.480 might have found that connection

NOTE Confidence: 0.9687901

00:44:10.480 --> 00:44:12.400 already. Okay. That's true. That's

NOTE Confidence: 0.9687901

00:44:12.400 --> 00:44:13.760 a good point. I've always

NOTE Confidence: 0.9687901

00:44:13.760 --> 00:44:14.960 looked, and you can tell

NOTE Confidence: 0.9687901

00:44:14.960 --> 00:44:16.260 where I'm going with this.

NOTE Confidence: 0.98748296

00:44:16.880 --> 00:44:18.640 I've always been asking and

NOTE Confidence: 0.98748296

00:44:18.640 --> 00:44:19.920 wondering the genes that are

NOTE Confidence: 0.98748296

00:44:19.920 --> 00:44:21.440 found. Could they have something

NOTE Confidence: 0.98748296

00:44:21.440 --> 00:44:22.560 to do with folding, with

NOTE Confidence: 0.98748296

00:44:22.560 --> 00:44:23.060 bending?

NOTE Confidence: 0.9040475

00:44:23.364 --> 00:44:25.225 What's interesting, Piezo one

NOTE Confidence: 0.9888553

00:44:25.525 --> 00:44:27.285 is a, you know, a

NOTE Confidence: 0.9888553

00:44:27.285 --> 00:44:28.265 touch bending,

NOTE Confidence: 0.9773353

00:44:28.725 --> 00:44:30.645 you know, gene. So that's

NOTE Confidence: 0.9773353

00:44:30.645 --> 00:44:32.085 kind of interesting. And that's

NOTE Confidence: 0.9773353

00:44:32.085 --> 00:44:33.605 the first one we found,

NOTE Confidence: 0.9773353

00:44:33.605 --> 00:44:34.805 right, of one of my

NOTE Confidence: 0.9773353

00:44:34.805 --> 00:44:35.305 families.

NOTE Confidence: 0.97623557

00:44:36.239 --> 00:44:37.520 And I think that's really

NOTE Confidence: 0.97623557

00:44:37.520 --> 00:44:39.360 interesting. So, yeah, that is

NOTE Confidence: 0.97623557

00:44:39.360 --> 00:44:40.239 always going to be my

NOTE Confidence: 0.97623557

00:44:40.239 --> 00:44:41.040 mind. The other thing I

NOTE Confidence: 0.97623557

00:44:41.040 --> 00:44:42.420 wanna bring up is that,

NOTE Confidence: 0.95476913

00:44:43.280 --> 00:44:44.640 two things. One is if

NOTE Confidence: 0.95476913

00:44:44.640 --> 00:44:45.600 you play a little game

NOTE Confidence: 0.95476913

00:44:45.600 --> 00:44:46.800 with yourself and ask the

NOTE Confidence: 0.95476913

00:44:46.800 --> 00:44:49.325 question, what does morph embryology

NOTE Confidence: 0.8907181

00:44:49.625 --> 00:44:51.645 do? What what creates morphology

NOTE Confidence: 0.71388817

00:44:51.945 --> 00:44:52.445 structure?

NOTE Confidence: 0.9978285

00:44:52.825 --> 00:44:53.945 It turns out that the

NOTE Confidence: 0.9978285

00:44:53.945 --> 00:44:55.224 number one tool in the

NOTE Confidence: 0.9978285

00:44:55.224 --> 00:44:55.724 toolbox

NOTE Confidence: 0.9961617

00:44:56.025 --> 00:44:58.364 is tissue folding, either invagination

NOTE Confidence: 0.9961617

00:44:58.585 --> 00:44:59.724 or branching morphogenesis.

NOTE Confidence: 0.9635879

00:45:00.344 --> 00:45:01.625 I mean, that's ninety percent

NOTE Confidence: 0.9635879

00:45:01.625 --> 00:45:02.744 of everything we are, from

NOTE Confidence: 0.9635879

00:45:02.744 --> 00:45:03.724 the first neurofold

NOTE Confidence: 0.99861

00:45:04.160 --> 00:45:05.780 to all the branching organs.

NOTE Confidence: 0.9935852

00:45:06.320 --> 00:45:07.840 So how many genes do

NOTE Confidence: 0.9935852

00:45:07.840 --> 00:45:09.760 you think control that? Cell

NOTE Confidence: 0.9935852

00:45:09.760 --> 00:45:10.260 proliferation,

NOTE Confidence: 0.99784696

00:45:11.040 --> 00:45:11.540 fusion,

NOTE Confidence: 0.953549

00:45:12.480 --> 00:45:14.180 bilayer, you know, deformation.

NOTE Confidence: 0.90130436

00:45:14.880 --> 00:45:16.660 That's everything. There probably

NOTE Confidence: 0.9955865

00:45:17.055 --> 00:45:18.494 thousands and thousands of genes

NOTE Confidence: 0.9955865

00:45:18.494 --> 00:45:19.454 that are involved with that

NOTE Confidence: 0.9955865

00:45:19.454 --> 00:45:20.655 process since that is the

NOTE Confidence: 0.9955865

00:45:20.655 --> 00:45:22.415 dominant tool that's in the

NOTE Confidence: 0.9955865

00:45:22.415 --> 00:45:22.915 toolbox.

NOTE Confidence: 0.9674231

00:45:25.855 --> 00:45:26.355 Yep.

NOTE Confidence: 0.9528036

00:45:26.815 --> 00:45:28.094 Well, there was a good

NOTE Confidence: 0.9528036

00:45:28.094 --> 00:45:29.614 model for maybe someone knows

NOTE Confidence: 0.9528036

00:45:29.614 --> 00:45:30.494 on this call. You you

NOTE Confidence: 0.9528036

00:45:30.494 --> 00:45:31.135 know what I mean? A

NOTE Confidence: 0.9528036

00:45:31.135 --> 00:45:32.900 genetics approach to doing this

NOTE Confidence: 0.9528036

00:45:32.900 --> 00:45:34.180 is to to do a

NOTE Confidence: 0.9528036

00:45:34.180 --> 00:45:36.340 CRISPR knockout screen. So if

NOTE Confidence: 0.9528036

00:45:36.340 --> 00:45:37.540 you if you know what

NOTE Confidence: 0.9528036

00:45:37.540 --> 00:45:38.739 phenotype you want, then you

NOTE Confidence: 0.9528036

00:45:38.739 --> 00:45:39.860 can ask the question, if

NOTE Confidence: 0.9528036

00:45:39.860 --> 00:45:41.060 I knock out that gene,

NOTE Confidence: 0.9528036

00:45:41.060 --> 00:45:42.820 does that phenotype vary? You

NOTE Confidence: 0.9528036

00:45:42.820 --> 00:45:43.940 know what I mean? So

NOTE Confidence: 0.9528036

00:45:43.940 --> 00:45:44.900 it it it's a question

NOTE Confidence: 0.9528036

00:45:44.900 --> 00:45:46.820 we can ask now because

NOTE Confidence: 0.9528036

00:45:46.820 --> 00:45:48.285 of our genetic toolbox that

NOTE Confidence: 0.9528036

00:45:48.285 --> 00:45:49.484 we can ask if the

NOTE Confidence: 0.9528036

00:45:49.484 --> 00:45:50.925 question is which genes that

NOTE Confidence: 0.9528036

00:45:50.925 --> 00:45:52.525 contribute to that. But you

NOTE Confidence: 0.9528036

00:45:52.525 --> 00:45:53.885 find the one that you

NOTE Confidence: 0.9528036

00:45:53.885 --> 00:45:54.765 know, you start with the

NOTE Confidence: 0.9528036

00:45:54.765 --> 00:45:55.645 one that has the best

NOTE Confidence: 0.9528036

00:45:55.645 --> 00:45:57.005 correlation with the inclusions, and

NOTE Confidence: 0.9528036

00:45:57.005 --> 00:45:57.964 that's the one we knock

NOTE Confidence: 0.9528036

00:45:57.964 --> 00:45:59.185 out first. Mhmm.

NOTE Confidence: 0.95016044

00:46:00.620 --> 00:46:01.739 Is there such thing as

NOTE Confidence: 0.95016044

00:46:01.739 --> 00:46:03.340 a Piazza one knockout, though?

NOTE Confidence: 0.95016044

00:46:03.340 --> 00:46:04.380 It just I think we

NOTE Confidence: 0.95016044

00:46:04.380 --> 00:46:05.980 don't exist without that gene.

NOTE Confidence: 0.95016044

00:46:05.980 --> 00:46:07.420 Right? I can't imagine. Do

NOTE Confidence: 0.95016044

00:46:07.420 --> 00:46:08.940 we? Is there a person

NOTE Confidence: 0.95016044

00:46:08.940 --> 00:46:10.640 that exists without that gene?

NOTE Confidence: 0.9245113

00:46:11.660 --> 00:46:12.860 Not sure. I'm not sure

NOTE Confidence: 0.9245113

00:46:12.860 --> 00:46:13.900 if there's a mouse model

NOTE Confidence: 0.9245113

00:46:13.900 --> 00:46:15.225 we eat on. So Yeah.

NOTE Confidence: 0.9245113

00:46:15.225 --> 00:46:16.265 Most of these, we knock

NOTE Confidence: 0.9245113

00:46:16.265 --> 00:46:17.405 it out. It's probably embryonic

NOTE Confidence: 0.9245113

00:46:17.465 --> 00:46:18.845 lethal. Yeah. Exactly.

NOTE Confidence: 0.9430607

00:46:19.225 --> 00:46:20.505 I would imagine that you

NOTE Confidence: 0.9430607

00:46:20.505 --> 00:46:21.965 know, because the first neurofold

NOTE Confidence: 0.9430607

00:46:22.105 --> 00:46:23.465 of creation of the heart

NOTE Confidence: 0.9430607

00:46:23.465 --> 00:46:24.985 is dependent on folding. So,

NOTE Confidence: 0.9430607

00:46:24.985 --> 00:46:26.105 you know Maybe we'd have

NOTE Confidence: 0.9430607

00:46:26.105 --> 00:46:27.145 to knock knock it out.

NOTE Confidence: 0.9430607

00:46:27.145 --> 00:46:28.780 We have to recreate whatever

NOTE Confidence: 0.9430607

00:46:29.000 --> 00:46:30.440 mutation we find in the

NOTE Confidence: 0.9430607

00:46:30.440 --> 00:46:31.880 patients that may recreate the

NOTE Confidence: 0.9430607

00:46:31.880 --> 00:46:33.420 same phenotype in the mouse.

NOTE Confidence: 0.9430607

00:46:33.560 --> 00:46:34.760 Mhmm. Mhmm. But one thing

NOTE Confidence: 0.9430607

00:46:34.760 --> 00:46:36.280 you could do, like, in

NOTE Confidence: 0.9430607

00:46:36.280 --> 00:46:37.400 some of these papers, if

NOTE Confidence: 0.9430607

00:46:37.400 --> 00:46:38.700 it's embryonic lethal

NOTE Confidence: 0.96390635

00:46:39.000 --> 00:46:40.200 or, yeah, important for early

NOTE Confidence: 0.96390635

00:46:40.200 --> 00:46:41.160 development, you can have a

NOTE Confidence: 0.96390635

00:46:41.160 --> 00:46:42.915 conditional knockout. You go, okay.

NOTE Confidence: 0.96390635

00:46:42.995 --> 00:46:44.355 We believe it's because of

NOTE Confidence: 0.96390635

00:46:44.355 --> 00:46:46.435 this tissue, and then then,

NOTE Confidence: 0.96390635

00:46:46.435 --> 00:46:47.715 you know, prove it via

NOTE Confidence: 0.96390635

00:46:47.715 --> 00:46:49.395 conditional knockout. Knock it out

NOTE Confidence: 0.96390635

00:46:49.395 --> 00:46:50.215 just in placenta.

NOTE Confidence: 0.98215085

00:46:50.915 --> 00:46:51.415 Yeah.

NOTE Confidence: 0.9560711

00:46:52.435 --> 00:46:53.475 But either knock it out

NOTE Confidence: 0.9560711

00:46:53.475 --> 00:46:54.915 just in placenta or, again,

NOTE Confidence: 0.9560711

00:46:54.915 --> 00:46:56.375 if we have a phenotype

NOTE Confidence: 0.9560711

00:46:56.435 --> 00:46:57.895 that maybe not a complete

NOTE Confidence: 0.9560711

00:46:57.930 --> 00:46:59.469 same, you know, null mutation

NOTE Confidence: 0.9560711

00:46:59.690 --> 00:47:01.130 phenotype that's a that's a

NOTE Confidence: 0.9653282

00:47:02.569 --> 00:47:03.950 based on just a mutation

NOTE Confidence: 0.9653282

00:47:04.010 --> 00:47:05.069 that makes it somehow

NOTE Confidence: 0.93211514

00:47:05.450 --> 00:47:07.869 function differentially, we could recreate

NOTE Confidence: 0.93211514

00:47:07.930 --> 00:47:09.290 that in the mouse model,

NOTE Confidence: 0.93211514

00:47:09.290 --> 00:47:10.430 see if we can recreate

NOTE Confidence: 0.93211514

00:47:10.650 --> 00:47:11.230 the phenotype.

NOTE Confidence: 0.99695617

00:47:13.945 --> 00:47:15.065 Alright. Again, I wanna thank

NOTE Confidence: 0.99695617

00:47:15.065 --> 00:47:16.425 everybody for your time. Please

NOTE Confidence: 0.99695617

00:47:16.425 --> 00:47:17.705 feel free to contact me,

NOTE Confidence: 0.99695617

00:47:18.025 --> 00:47:18.525 individually

NOTE Confidence: 0.9071069

00:47:19.065 --> 00:47:20.825 by email, either clinically or

NOTE Confidence: 0.9071069

00:47:20.825 --> 00:47:22.685 research, and, of course, Mankel,

NOTE Confidence: 0.9457347

00:47:23.785 --> 00:47:25.440 Ira, Hugh, you know, John,

NOTE Confidence: 0.9457347

00:47:25.440 --> 00:47:26.719 we I'm here, and I'm

NOTE Confidence: 0.9457347

00:47:26.719 --> 00:47:27.920 very excited to continue to

NOTE Confidence: 0.9457347

00:47:27.920 --> 00:47:28.960 work on this project with

NOTE Confidence: 0.9457347

00:47:28.960 --> 00:47:30.160 all of you. Yeah. Yeah.

NOTE Confidence: 0.9457347

00:47:30.160 --> 00:47:31.680 But definitely, thanks for the

NOTE Confidence: 0.9457347

00:47:31.680 --> 00:47:32.800 idea, Hugh. So,

NOTE Confidence: 0.9084785

00:47:33.200 --> 00:47:34.480 Harvey, we can follow-up on

NOTE Confidence: 0.9084785

00:47:34.480 --> 00:47:35.599 it if you want Andrew

NOTE Confidence: 0.9084785

00:47:35.599 --> 00:47:36.800 to do an analysis or

NOTE Confidence: 0.9084785

00:47:36.800 --> 00:47:38.099 one of your students analysis.

NOTE Confidence: 0.9084785

00:47:38.295 --> 00:47:39.015 Because I know you have

NOTE Confidence: 0.9084785

00:47:39.015 --> 00:47:40.535 the spreadsheet with some of

NOTE Confidence: 0.9084785

00:47:40.535 --> 00:47:42.135 those things quantitated. We could,

NOTE Confidence: 0.9084785

00:47:42.135 --> 00:47:43.655 you know, combine the two

NOTE Confidence: 0.9084785

00:47:43.655 --> 00:47:44.155 things.

NOTE Confidence: 0.998301

00:47:45.015 --> 00:47:45.515 Absolutely.

NOTE Confidence: 0.76059777

00:47:46.214 --> 00:47:46.954 Worth done.

NOTE Confidence: 0.93672174

00:47:48.216 --> 00:47:50.056 Alright. Great. Thanks, Harvey. Thank

NOTE Confidence: 0.93672174

00:47:50.056 --> 00:47:50.716 you, everybody.

NOTE Confidence: 0.94633037

00:47:51.496 --> 00:47:53.116 See you. Thank you, everyone.